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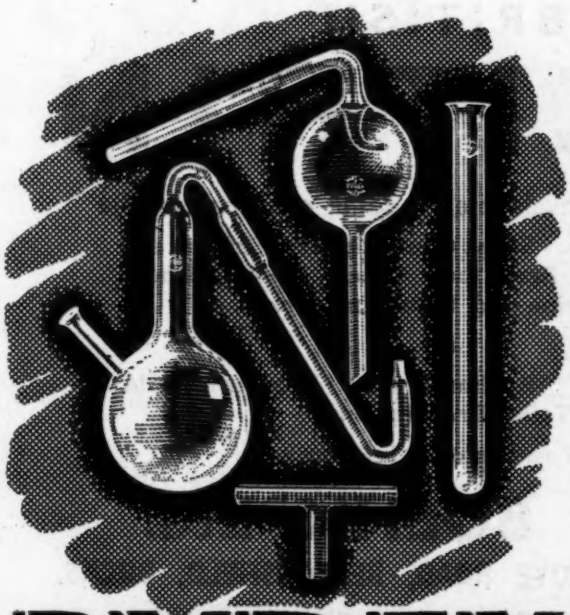

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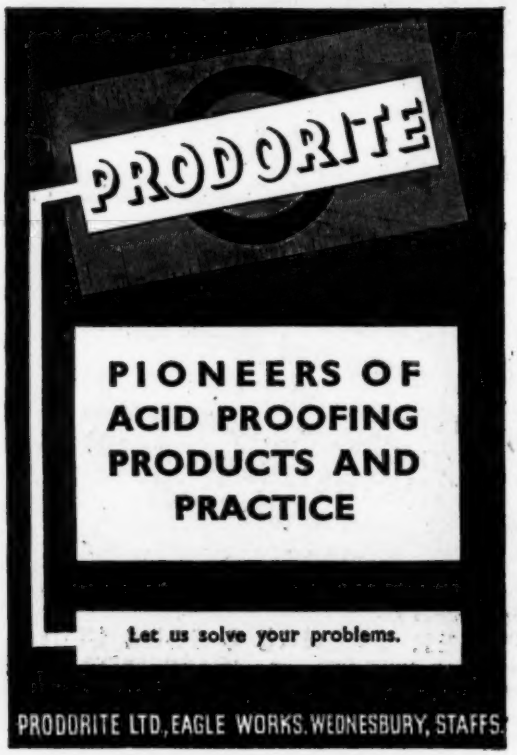
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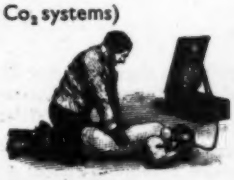

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Sames, K. See Ives, D. J. G.
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Smith, G. F. See also Dawson, H. M.
Spivey, E. See Milner, G.
Spring, F. S. See Ewen, E. S.
Stead, D. M. See Peters, A. T.
Sutton, D. A. See Farmer, E. H.
Todd, A. R. See Baddiley, J., and Kenner, G. W.
Topham, A. See Kenner, G. W.

Chemistry, gaining the Exhibition, and was second in Physics, being awarded the Neil Arnott medal. He took the D.Sc. degree in 1892.

Dufton was an active member of the Cambridge University Natural Science Club, to which he contributed six papers. Of these, the titles of two reflect his North Country upbringing; they are the "Metallurgy of Iron and Steel" and "Dyes and Dyeing." It was at this time that the present writer made Dufton's acquaintance and this ripened into friendship when we both acted as Junior Demonstrators (1891—1892) in the University Chemical Laboratory, especially as we had neighbouring benches in the Research Laboratory at which we spent the greater part of our time.

Dufton's first research work was carried out with S. Ruhemann, to whom many Cambridge men were deeply indebted not only for his careful training but also for his infectious enthusiasm. This work concerned itself with muconic acid and its derivatives (J., 1891, **59**, 26,760), thus mucic acid was converted into dichloromuconyl chloride by the action of phosphorus pentachloride in presence of the oxychloride.

In a short time, Dufton launched out on independent work. Having improved the methods for nitrating quinoline and perfected the separation of the 5- and the 8-nitroquinoline, he was in the position to prepare the corresponding amino- and hydrazino-compounds in reasonable quantity (J., 1891, **59**, 756; 1892, **61**, 782). The hydrazones of pyruvic acid only needed boiling for an hour with hydrochloric acid to undergo indole condensation giving excellent yields.

On leaving Cambridge, Dufton went back to his old school as Science Master. Writing in "The Bradfordian," Mr. H. E. Boothroyd says:

"Never shall we forget that tall, handsome, smiling young man, radiating happiness wherever he went, then, as all through his life.

"Even as schoolboys we thought his second name, Felix, singularly appropriate."

Dufton was not very long at Bradford, being appointed one of the first lot of Inspectors of Secondary Schools (Acland's Twelve Apostles). Research work had to be put aside and it was years before Dufton's name again appeared in scientific literature. Meanwhile he led a happy and useful life, becoming eventually Staff H.M.I. for Science in Secondary Schools. Mr. Boothroyd, a colleague in the Board of Education, bears witness in the notice already quoted, to Dufton's sympathetic help to secondary schoolmasters.

But Dufton never developed into the type of official who loses touch with the pursuit of science for its own sake and its bearing on everyday life. Chemists should be thankful for this; it was during the last war that he invented the distilling column which bears his name; an account was published shortly afterwards (*J. Soc. Chem. Ind.*, 1919, **38**, 45T; see also A. F. Dufton, J., 1921, **119**, 1988; 1922, **121**, 306). That one could get better results with a piece of apparatus one could make for oneself at small cost than with the fragile and expensive still-heads then in use, seemed too good to be true. But it was so.

Another of Dufton's activities was propaganda on behalf of economy of fuel. He frequently gave lectures on the subject; the present writer has recently read an address on "A Smokeless Leeds" given to the Leeds Luncheon Club (*Yorkshire Post*, November 20th, 1916) in which he advocates the increased use of gas, the cleaning of coal before coking, and complete abolition of bee-hive coke-ovens.

Dufton had been in failing health for some time; the end came suddenly; he was taken ill in his garden on June 24th, 1943, and died shortly afterwards.

He married Ellen Thornton, daughter of John Thornton of Leeds, in 1893. She survives him, with his daughter Lady Moran, and his son, Lieut.-Col. F. G. Dufton, Royal Engineers.

Our sympathy goes out to his widow and family, and the present writer regrets that meetings with Dufton were so infrequent since his Cambridge days.

J. T. Hewitt.

HAROLD GORDON RULE.

1887—1943.

H. Gordon Rule, D.Sc. (Edin.), Ph.D. (Munich), B.Sc. (London), Reader in Chemistry, University of Edinburgh, died on March 15th, 1943, after a long illness. He was one of three sons of the late Captain Thomas Rule, R.N. From Hillhead High School, Glasgow, Rule went to the Birkbeck College, London, and in 1909 graduated with first-class honours in chemistry. After a further year there, in which he engaged in research with Professor Alex. McKenzie, he proceeded to Baeyer's laboratory in Munich and worked under Professor Otto Dimroth on the problem of intramolecular transformations. Rule returned in 1912 to the Birkbeck College as an assistant and a year later was invited by Professor Sir James Walker to come to the University of Edinburgh, in which for thirty years he gave devoted service.

Rule's health did not permit his serving in the Navy as his father had done; but during the years of the Great War, in addition to arduous teaching duties and research for his D.Sc. thesis, he worked on problems of "national importance," such as the insulation of field telephone wire and the preparation of poison gases. The subject matter of his D.Sc. thesis appeared under the title "Amidine Salts and the Constitution of the so-called Iminohydrins" (J., 1918, **113**, 3). The combined application of physical and synthetic methods here described is typical of Rule's subsequent work.

The opening of the spacious new Chemistry Department at King's Buildings shortly after the end of the

War offered Rule great opportunities as head of the Organic Chemistry Department, in the planning of which he gave Sir James Walker invaluable help. Moreover on the institution of the Ph.D. degree in the Scottish Universities a steady stream of post-graduate students came to work under the active supervision and inspiring guidance of Rule. Within the next twenty years some sixty contributions (mostly to the Society) testified to his industry and that of his students. Mention should be made of his paper entitled " Optical Activity and the Polarity of Groups attached to the Asymmetric Atom " (J., 1924, **125**, 1121), which introduced a series of some thirty papers dealing with the factors governing the magnitude of optical rotatory power in which Rule showed conclusively the prime importance of the nature of the polar groups in asymmetric molecules and also in the solvents employed. Much of Rule's work is summarised in a paper which, at the request of the late Professor Lowry, he read at the Faraday Society General Discussion upon Optical Activity (see *Trans. Faraday Soc.*, 1930, **26**, 321).

In later years Rule turned to the study of benzanthrone and allied compounds and, successfully overcoming formidable experimental difficulties, obtained many interesting results. In one of his last papers, however, he returned to the subject of optical activity and with G. M. Henderson published an account of the first complete resolution of a racemic compound by chromatographic adsorption (J., 1939, 1568).

All Rule's work was characterised by thoroughness and precision. His lectures were prepared with great care and always kept up to date. His gentle manner and quiet sense of humour endeared him to his students.

His translation of Julius Schmidt's " Organische Chemie " was first published in 1926 and has now reached its fourth edition. This English version of " Schmidt " is not merely a translation of the original volume: many of the chapters were rewritten by Rule and later editions contained excellent summaries by him on such topics as chromatographic adsorption, steroids, vitamins, plastics, etc.

As previously mentioned, Rule was physically not strong and in 1922–23 he was incapacitated for a year and a half by rheumatic fever, which left him with a weak heart. Barred in consequence from active exercise, he enjoyed motoring and took special pleasure in driving through the countryside associated with Walter Scott and Robert Louis Stevenson.

In 1919 he married Elizabeth Cairns Rutherford, M.A., B.Sc., who gave him invaluable help in the preparation of the several editions of Schmidt, and devotedly nursed him during his long illnesses. The sympathy of Rule's many friends goes to her in her great bereavement.

JOHN E. MACKENZIE.
NEIL CAMPBELL.

RAYMOND TAYLOR.

1890—1943.

RAYMOND, third son of the late Frederick Taylor of Samuel Taylor and Company, the well-known Stourbridge chain and anchor manufacturers, was born at Brierley Hill, Staffordshire, on March 8th, 1890. He received his early education at Wolverhampton Grammar School, from which he won an open exhibition to Queens' College, Cambridge, in 1909. Two years later he obtained a First Class in Part I of the Natural Sciences Tripos and became a scholar of Queens'. Specialising in chemistry, he went on to Part II in 1913 and was placed in the second class. Before the outbreak of war he held an appointment as chemist at the iron and steel works of Messrs. Sanderson and Co., Middlesborough, but he relinquished this to enlist in the Royal Army Medical Corps. Obtaining a commission shortly after, he was first posted to the Durham Light Infantry, but on account of his scientific training he was later transferred to the Special Brigade of the Royal Engineers, newly formed for the prosecution of gas warfare. During 1915—16 he saw active service in France, where he was badly gassed by phosgene. Upon recovery he was passed for light duty only, owing to a permanent injury to the heart, and was sent to the Royal College of Science to work under Professor H. B. Baker on problems connected with gas warfare. On discharge in 1919, Taylor took up a post with Messrs. Albright and Wilson, Oldbury, but in 1921 he resigned to commence his long association with the Department of Scientific and Industrial Research.

His first assignment was to study the direct chlorination of methane and the initial academic work was carried out at Oxford under the supervision of Dr. D. L. Chapman. During this period Taylor was a member of Jesus College. The results of the investigation were embodied in a thesis for which he received the research degree of B.Sc. in 1922. For the purpose of carrying out large-scale work on the same subject, he was posted to the Royal Naval Cordite Factory, Holton Heath, where, remaining till the end of 1925, he was associated also with an investigation of methods for concentrating aqueous formaldehyde solutions. His last move was to the then newly-established Chemical Research Laboratory at Teddington, where, under the late Sir Gilbert Morgan, he was responsible for the development of researches involving the use of gases under high pressure. It was in this field, while studying the synthesis of methanol from carbon monoxide and hydrogen, that Taylor made what was probably his outstanding discovery, namely, that a notable proportion of ethyl alcohol could be obtained by suitable modification of the catalyst. On the basis of carbon content, up to 50% of the liquid product was isolable as ethyl alcohol, but unfortunately about half of the reacting carbon monoxide was simultaneously converted into methane. Outside of high pressure reactions, Taylor had many other chemical interests. He was early concerned in an investigation of Empire sources of helium, and developed a method

for the dry assay and isolation of that gas from Travancore monazite. He also studied various addition compounds of boron trifluoride with organic esters, the azeotropic dehydration of alcohols with carbon tetrachloride, and an interesting thiocarbonyl of iron. The results of these and other investigations are described mainly in the publications of the Royal Society, the Chemical Society and the Society of Chemical Industry. Taylor was elected a Fellow of the Chemical Society in 1926 and a member of the Society of Chemical Industry in 1929. During 1940—41 he was Honorary Secretary of the committee of the London Section of the Society of Chemical Industry, and thereafter he remained a member of this committee up to the time of his death.

Among a wide circle of friends, Taylor will be remembered not only for his distinguished presence and courtly manner, but also for his utter selflessness and outstanding desire to serve. Although of great ability, he was somewhat reserved and showed great deference to the views of others. To his intimates, he was a tower of strength and his counsel was much sought after and valued. Taylor was a firm believer in the power of good and a great exponent of neighbourly duty. As an example may be cited his humanitarian work in the relief of Czech and Sudeten refugees; not only did he provide sanctuary for several, but he was personally instrumental in facilitating the escape of some of their relatives to this country. It is not too much to say that some of these refugees owe their lives to his efforts. This same desire to serve prompted him to become one of the earliest Air Raid Wardens in the Borough of Twickenham, and he remained an active civil defence worker to the end.

Essentially a lover of the beautiful, Taylor revelled in the open country, particularly the Cotswolds and North Wales, and was no lesss keen in his appreciation of flowers and foliage, the arts and the work of the craftsman and, not unnaturally, he was also a music lover. In 1915, he married Nettie Turquand, by whom, with their children Margaret (now Mrs. Ashley Bramall) and Paul he is survived. In recent years Taylor took a natural pride and a lively interest in his wife's many activities as a Councillor of the Borough of Twickenham.

He died on January 24th, 1943, after a brief but painful illness, endured with characteristic fortitude.

D. V. N. Hardy.

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135. *The Determination of Dissociation Constants of Monobasic Acids. Part II. The Extrapolation Method.*

By D. J. G. Ives and K. Sames.

An extrapolation method previously proposed is shown to apply accurately to conductivity measurements which are free from systematic errors, and to provide a very accurate interpolation equation of great value in the determination of cell constants. The use of benzoic acid, instead of the usual potassium chloride, is recommended as the standard electrolyte for this purpose. The effect of certain errors on the extrapolation method is discussed.

In a previous paper (Ives, J., 1933, 731; to be considered as Part I), a method was proposed for calculating the equivalent conductivity at zero concentration and the thermodynamic dissociation constant of a weak electrolyte from conductivity data. The method was based on Ostwald's dilution law, Onsager's ionic mobility equation (*Physikal. Z.*, 1927, **28**, 277), and the Debye–Hückel activity equation (*ibid.*, 1923, **24**, 185); and was shown to be capable of giving true dissociation constants independently of the absolute accuracy of the conductivity measurements and without reference to any recorded ionic mobility data. Fuoss and Kraus (*J. Amer. Chem. Soc.*, 1933, **55**, 476), just previously, had also devised a method for solving the same problem, and other modifications, designed to facilitate computation, have been suggested (Fuoss, *ibid.*, 1935, **57**, 488; Shedlovsky and Uhlig, *J. Gen. Physiol.*, 1934, **17**, 549; Shedlovsky, *J. Franklin Inst.*, 1938, **225**, 739).

The sensitivity to various experimental errors of the equation

$$\Lambda + aC_i^{\frac{1}{2}} = \Lambda_0 - \Lambda^2 C \times 10^{-2AC_i^{\frac{1}{2}}}/K(\Lambda_0 - aC_i^{\frac{1}{2}}) \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

(Ives, *loc. cit.*), where a and A are the constant of the Onsager and the Debye–Hückel equation respectively, and the other symbols have their usual significance, has been studied in detail by Kilpatrick (*J. Chem. Physics*, 1940, **8**, 306), with confirmation of the properties originally claimed for this equation. Other similar methods have been examined by Belcher (*J. Amer. Chem. Soc.*, 1938, **60**, 2744). It is now established that these extrapolation methods can be applied satisfactorily to the determination of true dissociation constants and are of unique value when no independent ionic mobility values are available, as in the study of many non-aqueous solutions, and in certain other special cases (see following paper). Restrictions are imposed by the failure of the Debye–Hückel and the Onsager limiting equation at higher concentrations; the use of empirical extensions of these equations is not generally advisable. Nevertheless, equation (1) applies with considerable accuracy up to concentrations of the order of 3—5 $\times$ 10^{-3} equiv./l., within a range in which very precise measurements can be made with modern conductivity methods.

The validity of the equation can be tested in two ways. In the above form it can be used for the extrapolation of conductivity data and the determination of Λ_0 and K, which can be compared with the values obtained by the ordinary methods. Alternatively, it can be rearranged into

$$\Lambda = [-K\Lambda_x + \Lambda_x\sqrt{K(K + 4C \times 10^{-2AC_i^{\frac{1}{2}}})}]/2C \times 10^{-2A\sqrt{C_i}} \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $\Lambda_x = \Lambda_0 - aC_i^{\frac{1}{2}}$, and used to calculate values of equivalent conductivity at any concentration, C,

from Λ_0 and K determined by the usual methods. Calculated and experimental values of Λ can then be compared. The results of such tests are shown in the following table, the data used being those of Shedlovsky (*J. Amer. Chem. Soc.*, 1932, **54**, 1411) and of Brockman and Kilpatrick (*ibid.*, 1934, **56**, 1483) on acetic and benzoic acids respectively.

Acetic acid.

	Obs.	Calc.
$K \times 10^5$	1·753	1·747
Λ_0	390·59	391·02

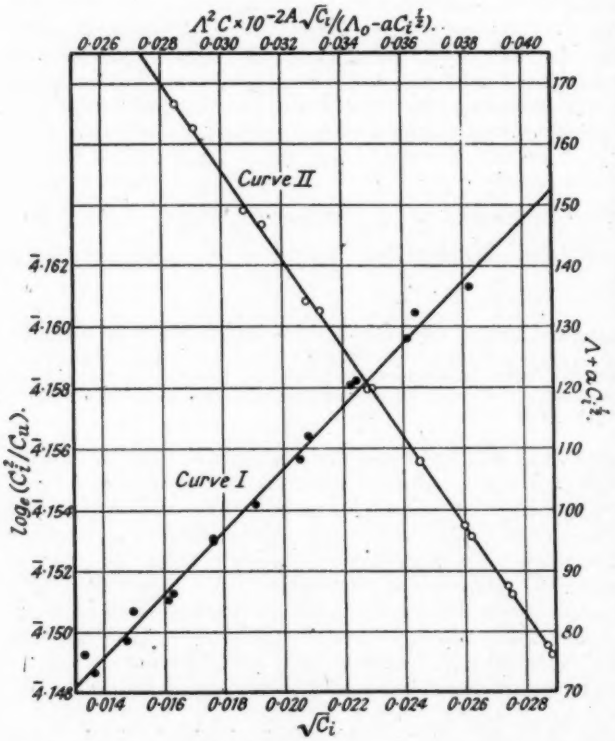
$C \times 10^4$.	Λ, obs.	Λ, calc.	$C \times 10^4$.	Λ, obs.	Λ, calc.
34·4065	27·19	27·21	2·1844	96·47	96·52
24·1400	32·21	32·23	1·5321	112·02	112·09
13·6340	42·215	42·22	1·1135	127·71	127·68
10·2831	48·13	48·16	0·2801	210·32	210·35

Benzoic acid.

	Obs.	Calc.
$K \times 10^5$	6·312	6·314
Λ_0	382·10	382·05

$C \times 10^4$.	Λ, obs.	Λ, calc.	$C \times 10^4$.	Λ, obs.	Λ, calc.
10·729	82·94	82·93	3·8108	127·85	127·85
9·9902	85·54	85·54	2·6281	147·66	147·66
7·6027	96·20	96·19	2·1148	160·14	160·09
3·9045	126·60	126·61	1·9112	166·03	166·07
			0·95887	209·32	209·31

It will be seen that the agreement between Λ, obs. and Λ, calc. at the experimental concentrations is of the highest order of accuracy. There can be no doubt that equation (2) expresses the conductivity of weak uni-univalent electrolytes, within a restricted concentration range, and in the absence of disturbing factors, with very considerable precision. It is strongly urged that this equation, applied to the above data for benzoic acid, provides the best available means of calibrating conductivity cells of low constant, since it permits the accurate interpolation of one of the best series of conductivity measurements which have been made. The equation can be solved for Λ by a fairly simple series of successive approximations. The great advantages of benzoic acid over the usual potassium chloride as a standard electrolyte are immediately obvious. This easily purified, non-hygroscopic substance of low density is a weak electrolyte; the gradient of its specific conductivity–concentration curve is much less than that of a strong electrolyte, the concentrations of the calibration solutions are correspondingly greater, and no solvent correction is necessary. It is clear that these properties provide a very substantial gain in accuracy and ease of manipulation, and facilitate the desirable procedure of covering the widest possible resistance range in the calibration experiments.



A source of error in the application of equation (1) to extrapolation has not hitherto been mentioned. Although an absolute error of 1% in the conductivity measurements has a negligible effect on the value of the dissociation constant obtained (Ives; Kilpatrick; *locc. cit.*), a non-uniform error, affecting one conductivity range more than another, is very much more significant. An error of this type is likely to arise from the direct earthing of the bridge circuit, and the Wagner earthing system (*Z. Elektrochem.*, 1926, **32**, 1001; Jones and Josephs, *J. Amer. Chem. Soc.*, 1928, **50**, 1049; Shedlovsky, *ibid.*, 1930, **52**, 1793) has been designed to deal with this difficulty. Nevertheless, the direct earth is in frequent use, and the errors produced are generally far too small seriously to affect ordinary conductivity measurements and calculations. If, however, extrapolation methods are to be applied to the conductivity measurements, the situation is entirely different, because these methods are peculiarly sensitive to errors of this kind, to a greater extent the weaker the electrolyte and the longer the extrapolation. The conductivity results reported in Part I (*loc. cit.*) were adversely affected in this manner: the dissociation constant of benzoic acid was found to be $6{\cdot}53 \times 10^{-5}$, a result confirmed in repeated experiments carried out under the same conditions, but which is in poor agreement with the value for this constant which must now be accepted ($6{\cdot}312 \times 10^{-5}$, Brockman and Kilpatrick, *loc. cit.*; $6{\cdot}295 \times 10^{-5}$, Saxton and Meier, *J. Amer. Chem. Soc.*, 1934, **56**, 1919; $6{\cdot}373 \times 10^{-5}$, Jeffery and Vogel, *Phil. Mag.*, 1934, **18**, 901; $6{\cdot}27 \times 10^{-5}$, Dippy and Williams, J., 1934, 1888). The measurements reported in the following paper were carried out under the same conditions and will also be subject to this error, which will, however, be negligible in the case of acids with dissociation constants greater than 10^{-3} (cf. Belcher, *loc. cit.*), and probably significant in only one of the cases studied.

A test for constant conductivity errors has been suggested by Kilpatrick (*loc. cit.*) in the linearity of the plot of $\log_{10}(C_i^2/C_u)$ against $C_i^{\frac{1}{2}}$; the application of this to the case of *trans*-1-cyano*cyclo*hexane-2-carboxylic acid ($K = 1{\cdot}365 \times 10^{-4}$) is shown in curve I in the figure. The points are experimental and the continuous line has the theoretical Debye–Hückel slope. Curve II is a graphical representation of equation (1), and should, of course, be strictly linear. Since the result of this test is reasonably satisfactory, the new dissociation-constant data are advanced as being accurate to within 2%, and probably considerably better than this in the case of the stronger acids.

The authors record their thanks to Mr. W. J. Allum for helpful discussions in connexion with conductivity errors.

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[*Received, May 28th,* 1943.]

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136. *The Determination of Dissociation Constants of Monobasic Acids. Part III. The Strengths of Some Cyano-acids.*

By D. J. G. IVES and K. SAMES.

Thermodynamic dissociation constants of some cyano-substituted carboxylic acids have been measured by a conductivity method, the extrapolation equation discussed in the preceding paper being used. The results are considered in relation to the structure of the cyano-acids and are correlated with existing data on the influence of substituents on acid strength. A connexion between the dipole moment of the substituent and the dissociation constant of the acid is proposed, which can be applied only when the influence of the substituents is purely inductive in nature and when the effect of free rotation of bonds need not be considered.

THE cyano-group has received comparatively little attention in studies of the effects of polar substituents on acid strengths, in spite of the fact that it is particularly interesting because of its halogenoid nature but *m*-directing influence in benzene substitution. The preparation of a number of cyano-substituted carboxylic acids is now described. In general, they are fairly easily hydrolysed to the corresponding amic acids, a tendency which might be an obstacle to the determination of their dissociation constants by the usual methods. These determinations have been carried out by measurement of conductivities of dilute aqueous solutions of the acids, and dissociation constants have been calculated by the extrapolation method (cf. preceding paper), which does not require the preparation of sodium salts. The range of acids has been limited by difficulties of preparation and purification, and the available data are summarised below, and discussed in three sections.

Acid.	$K \times 10^5$.	Acid.	$K \times 10^5$.
Cyanoacetic	342	*cyclo*Hexylcyanoacetic	430
β-Cyanopropionic	10·2	Dimethylcyanoacetic	380
γ-Cyano-*n*-butyric	3·66	*trans*-1-Cyano*cyclo*hexane-2-carboxylic	13·65

[The only previously recorded dissociation constant is that of cyanoacetic acid ($3{\cdot}73 \times 10^{-3}$, Ostwald, *Z. physikal. Chem.*, 1889, **3**, 170; $3{\cdot}63 \times 10^{-3}$, Wightman and Jones, *Amer. Chem. J.*, 1911, **46**, 56; $3{\cdot}49 \times 10^{-3}$, Kendall, J., 1912, **101**, 1275, recalculated by MacInnes, *J. Amer. Chem. Soc.*, 1926, **48**, 2068; $3{\cdot}36 \times 10^{-3}$, Saxton and Darken, *ibid.*, 1940, **62**, 847).]

ω-Substituted n-*Aliphatic Acids.*—For purposes of comparison, dissociation constants ($\times 10^5$) of terminally substituted acetic, propionic, and *n*-butyric acids are collected below. Since the absolute accuracy of these figures is not of importance, they are, unless otherwise stated, the "classical" values taken from Scudder, "The Electrical Conductivity and Ionization Constants of Organic Compounds," 1914.

R.	$CH_2R{\cdot}CO_2H$.	$CH_2R{\cdot}CH_2{\cdot}CO_2H$.	$CH_2R{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$.
H	1·753 (*a*)	1·336 (*b*)	1·50 (*b*)
F	213 (*c*)	—	—
Cl	139·7 (*d*)	10·1 (*e*)	3
Br	138	9·8	2·6
I	71	9·0	2·3
CN	342 (*f*)	10·2 (*f*)	3·66 (*f*)
CO_2H	149 (*g*)	6·41 (*g*)	4·53 (*g*)

References.—(*a*) Shedlovsky, *J. Amer. Chem. Soc.*, 1932, **54**, 1411; (*b*) Harned and Ehlers, *ibid.*, 1933, **55**, 2379; (*c*) Swarts, *Bull. Sci. Acad. roy. Belg.*, 1922, **8**, 343; (*d*) MacInnes, Shedlovsky, and Longsworth, *Chem. Rev.*, 1933, **13**, 29; (*e*) Dawson, Hall, and Key, J., 1928, 2844; (*f*) present paper; (*g*) Gane and Ingold, J., 1931, 2153.

Cyanoacetic acid is seen to be much stronger than the halogeno-acids. This might be attributed, at first sight, to the very powerful inductive effect of the CN group, which has a bond moment greatly exceeding those of C–Hal. This explanation does not hold, however, when interatomic distances are taken into account, since the primary moment in the cyano-acid is considerably farther away from the acidic hydrogen than in the other cases. The strength of β-cyanopropionic acid does not indicate any such predominance of inductive effect for the cyano-group. Quantitative correlations between dipole moments of substituents and ionisation constants have been developed (Waters, *Phil. Mag.*, 1929, **8**, 436; Smallwood, *J. Amer. Chem. Soc.*, 1932, **54**, 3048; Schwartzenbach and Egli, *Helv. Chim. Acta*, 1934, **17**, 1184; Schwartzenbach and Epprecht,

ibid., 1936, **19**, 493; Nathan and Watson, J., 1938, 890; Westheimer and Shookhoff, *J. Amer. Chem. Soc.*, 1939, **61**, 555, 1977, etc.), but a simple treatment, for comparative purposes only, is now suggested for acids which are closely similar in type. All such calculations require an assumption as to the location of the carboxylic hydrogen atom, and, as a simplifying approximation, it has been assigned to a position on the extension of the line joining the α- and the carboxylic carbon atom, 1·45 A. beyond the latter (Kirkwood and Westheimer, *J. Chem. Physics*, 1938, **6**, 506). The following dimensions have been used: covalent atomic radii, C, 0·77; F, 0·64; Cl, 0·99; Br, 1·14; I, 1·33 A.; CN bond length, 1·16 A.; and the tetrahedral angle of 109° 28′. The vector components of the field at the carboxylic hydrogen atom, due to the substituent dipole, $E_x = \mu(3\cos^2\theta - 1)/\varepsilon r^3$ and $E_y = \mu(3\sin\theta\cos\theta)/\varepsilon r^3$ (where μ is the moment of the primary dipole, θ the angle between the dipole axis and the line joining it to the hydrogen atom, r the length of this line, and ε the dielectric constant of the medium), parallel and perpendicular respectively to the dipole axis, have been resolved along the axis of the carboxyl group (cf. Groves and Sugden, J., 1937, 1992). The primary dipole is assumed to be dimensionless and situated midway between the parent atoms. Since we are concerned with the effect of the substitution of a group for hydrogen, the dipole is taken as equal in moment to that of the corresponding substituted methane and, because the calculations have no absolute significance, the dielectric constant of the medium has been taken as unity. The results are shown below.

X.	μ of CH_3X.	r, A.	θ.	E.	pK, calc.	pK, obs.	Δ.
F	1·81 (*a*)	2·32	53° 54′	0·197	2·70	2·67	0·03
Cl	1·87 (*b*)	2·43	50° 34′	0·190	2·77	2·85	−0·08
Br	1·80 (*b*)	2·48	49° 13′	0·177	2·91	2·86	0·05
I	1·64 (*b*)	2·54	47° 36′	0·153	3·16	3·15	0·01
CN	3·94 (*b*)	3·36	33° 59′	0·174	2·98	2·47	0·51

References. (*a*) Smyth and McAlpine, *J. Chem. Physics*, 1934, **2**, 499; (*b*) Groves and Sugden, J., 1937, 158.

The component of the dipole field along the carboxyl axis, in a direction to facilitate the ionisation of the hydrogen atom, is shown under E (col. 5). If the influence of the polar substituent on the strength of the acetic acid is solely electrostatic in origin, and if the component of the field in this single direction is alone significant, these figures indicate that cyanoacetic should be about equal in strength to bromoacetic acid. These assumptions are supported for the halogen acids in the following manner. The field is multiplied by the electronic charge and by a distance, d, in order to obtain a quantity with the dimensions of energy; application of the isotherm would then give ΔpK, defining, in the usual terms, the difference in strength between the unsubstituted and substituted acids. The converse calculation has been carried out for the halogeno-acids, d being calculated from the known values of ΔpK. The results for the fluoro-, chloro-, bromo-, and iodo-acids are 0·209, 0·197, 0·212, and 0·207 A., respectively. This quantity can have little real significance: it will depend inversely on the effective dielectric constant assumed for the medium and will, in effect, contain the various uncertainties associated with the problem. It is, however, of suitable magnitude for, and may be plausibly pictured as, a distance through which the carboxylic hydrogen atom must be withdrawn from the molecule before it can separate as a hydrion. The remarkable constancy of the value of d for the four acids leads to the tentative inference that the substitutional effects are in these cases predominantly electrostatic. A mean value of 0·206 A. for d leads to the calculated pK values shown in col. 6 of the foregoing table, and these may be compared with the known values in col. 7, the differences being shown in the last column. There must, of course, be general agreement in the case of the halogen acids, but it is noteworthy that the results are self-consistent and show no systematic deviations. Cyanoacetic acid, on the other hand, shows a very considerable discrepancy, and it is suggested that this acid is abnormally strong owing to the operation of a factor of a different kind. The same conclusion may be reached if internally transmitted inductive effects are considered; the additional carbon atom interposed in the cyano-acid would reduce any such effect by a factor of the order of 0·02 (Waters, J., 1933, 1551), much more than sufficient to counterbalance the greater primary dipole.

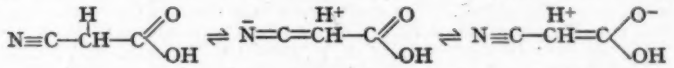
A reason for this enhancement in strength can be found in the polarisability (or, possibly, mesomeric polarisation) of the nitrile group, $N\overset{\curvearrowleft}{\equiv}C{-}CH_2{-}CO_2H$. There is no direct tautomeric path by which this can be transmitted to the carboxyl group, but it may be relayed inductively in the manner suggested by Dippy, Watson, and Williams (J., 1935, 346), and may be compared with the enhancement in strength found in vinylacetic acid ($K = 4{\cdot}48 \times 10^{-5}$; Ives, Linstead, and Riley, J., 1933, 561) and in phenylacetic acid ($K = 4{\cdot}88 \times 10^{-5}$; Dippy and Williams, J., 1934, 161) as compared with acetic acid ($K = 1{\cdot}753 \times 10^{-5}$). It may be noted that the ΔpK values in these two cases (0·41 and 0·44, respectively) are of the same order of magnitude as the difference between observed and calculated pK's for cyanoacetic acid (0·51).

Such an effect is considerably reduced when an additional methylene group is interposed (β-phenylpropionic acid, $K = 2{\cdot}19 \times 10^{-5}$, Dippy and Lewis, J., 1937, 1008; Δ^{γ}-pentenoic acid, $K = 2{\cdot}10 \times 10^{-5}$, Ives, Linstead, and Riley, *loc. cit.*; cf. propionic acid, $K = 1{\cdot}335 \times 10^{-5}$, Dippy, *loc. cit.*), and it is found that β-cyanopropionic acid is not significantly stronger than the β-halogenated acids. A similar calculation to the above has been applied to the propionic acids, assuming them to exist predominantly in the *trans*-configuration, and adopting a value for d of 0·328 A. The results are shown on p. 515. The cyano-acid is, if anything, slightly weaker than would be anticipated in this case.

X.	r, A.	θ.	E.	pK, calc.	pK, obs.	Δ.
Cl	3·68	23° 14′	0·0575	3·92	4·00	−0·08
Br	3·75	22° 47′	0·0529	3·99	4·01	−0·02
I	3·84	22° 14′	0·0455	4·12	4·05	0·07
CN	4·85	17° 26′	0·0599	3·88	3·99	−0·11

An analogy with the cyano-acids can be found in the dicarboxylic acids, the primary dissociation constants of which are included in the table on p. 513. Malonic acid (regarded as α-carboxyacetic acid) is relatively stronger, compared with the β-carboxylic acid (succinic), than would be anticipated from a purely inductive effect. This can clearly be seen from the ratio K_α/K_β, which, for the various substituted acids, has the values Cl, 15; Br, 14; I, 8; CN, 33; CO_2H, 23: the two groups which are *m*-directing in benzene substitution have notably larger values of this ratio. This is all the more significant when it is remembered that the relative decrease in field strength at the ionisable hydrogen atom resulting from the intercalation of successive methylene groups is much less in these two cases than in the others, because the initial distance from the primary dipole in the α-acid is considerably greater. This factor would tend to reduce the difference in acid strength between the homologues and is, indeed, distinguishable in the slightly greater relative strengths of glutaric and γ-cyano-*n*-butyric acids (see p. 513).

The Effect of Alkyl Substitution.—Dimethylcyanoacetic acid is appreciably stronger than cyanoacetic acid, an unexpected result in view of the electron-release function of methyl groups, but in accordance with the Thorpe–Ingold valency deflexion hypothesis. If dimethyl substitution causes a decrease in the valency angle between the cyano- and the carboxy-group of the order of 2°, it can be shown that such an increase in strength would result. Recent work has shown, however, that such an explanation must be accepted with reserve (Westheimer and Shookhoff, *J. Amer. Chem. Soc.*, 1939, **61**, 555) and an alternative interpretation appears to merit consideration. Comparison can be made with the analogous pair of malonic acids: the four dissociation constants (× 10^5) are: cyanoacetic, 342; dimethylcyanoacetic, 380; malonic, 149; dimethylmalonic, 68·3: the effects of dimethyl substitution are opposite in the two cases. The polarisation of the cyano-group enhances acid strength in the manner already suggested, but it also promotes lability of the methylene hydrogen atoms, which are well known to be abnormally reactive. It may be suggested that the cyanoacetic acid molecule is degenerate, involving the resonance forms (I), (II), and (III), of which (III) is likely to be more significant than (II), and clearly leads to a distribution of charges unfavourable to the



(I.) (II.) (III.)

ionisation of the carboxylic hydrogen. It might be said, alternatively, that the methylene activation has a depressing effect on acid strength because it partly "short circuits" the influence of the cyano-group in promoting ionisation. In dimethylcyanoacetic acid, however, such activation, and the resonance of which it is the result, cannot occur, and the full effect of the cyano-group is transmitted to the carboxylic hydrogen atom. The situation is not quite the same in the case of the malonic acids because the resonance state must be symmetrical and any unfavourable charge which develops must be distributed between two carboxyl groups. The influence of any dipole must be self-cancelling because of the statistical factor; either one group or the other may ionise. The strength of malonic acid is therefore not appreciably depressed by resonance, and dimethyl substitution produces the expected decrease in strength because of the electron-releasing properties of the methyl groups.

The greater strength of *cyclo*hexylcyanoacetic acid than of cyanoacetic (430 × 10^{-5} and 342 × 10^{-5}, respectively) is more marked, and may be associated with the introduction of a large polarisable group: it is paralleled by the greater strength of *cyclo*hexylacetic than of acetic acid (2·36 × 10^{-5}, Zelinsky and Izgarysev, *J. Russ. Phys. Chem. Soc.*, 1908, **40**, 1379, and 1·753 × 10^{-5}, respectively). Comparisons of this kind, however, between acids differing considerably in structure and dimensions may be invalidated by differences in entropy of ionisation (cf. Hammett, *J. Chem. Physics*, 1936, **4**, 613); *e.g.*, the large increase in the size of the anion in this case may cause a smaller decrease in entropy owing to orientation of water molecules in solution. Other steric factors may also be significant (cf. Brown and Bartholomay, *ibid.*, 1943, **11**, 43). All discussions of minor differences in acid strength are subject to these uncertainties.

trans-1-*Cyano*cyclo*hexane*-2-*carboxylic Acid.*—Preparative difficulties have precluded the comparison of *cis*- and *trans*-modifications of this acid with each other and with the rigid-ring *cyclo*pentane analogues. In one of the possible strainless forms of the *trans*-acid, it can be shown that the N≡C–CH–CH–CO_2H skeleton will lie in one plane in the *trans*-configuration; it is considered that dipole interaction will strongly favour this particular strainless form. Applying the method of calculation already described, and using the same value for the distance *d* as for the substituted propionic acids and $K = 1{\cdot}28 \times 10^{-5}$ for the corresponding unsubstituted acid (hexahydrobenzoic acid, Scudder, *loc. cit.*), we obtain pK = 3·90. This compares very well with the observed value of 3·86, and this agreement may be taken as supporting the predominant *trans*-configuration of the propionic acids: a *cis*-configuration would involve a very great increase in strength of the cyano-acid. A comparison with the dicarboxylic acids may be made in confirmation of this conclusion. The primary dissociation constant of succinic acid (6·41 × 10^{-5}; Gane and Ingold, *loc. cit.*) is much closer to that of *trans*-

hexahydrophthalic acid ($6{\cdot}61 \times 10^{-5}$) than of the *cis*-acid ($4{\cdot}57 \times 10^{-5}$; Kuhn and Wassermann, *Helv. Chim. Acta*, 1928, **11**, 50). Mills (*Reports Inst. Solvay*, 1931) has suggested that succinic acid has the *trans*-form in its equilibrium conformation, and it is to be expected that it will be simulated in this respect by its half-nitrile.

Experimental.

Conductivity Measurements.—The apparatus and method were similar to those described by Ives and Riley (J., 1931, 1998). All measurements were made at 25°, and all the solutions were prepared with water of specific conductivity $0{\cdot}15$—$0{\cdot}30 \times 10^{-6}$ ohm^{-1}, obtained from a Stuart and Wormwell still (J., 1930, 85). Suitable precautions were adopted to prevent the uptake of moisture by hygroscopic solutes during weighing. At least two series of measurements were carried out with each acid, samples being either from independent preparations or from successive crystallisations. In all cases one of the measured solutions was kept in the conductivity cell overnight in order to detect any solvolytic reaction which might have invalidated the treatment of the results. No such reaction was found in any case. The results are tabulated below, data for one acid being given in full in order to indicate the degree of concordance obtained, and Λ_0 values for each series of runs of the other acids.

Cyanoacetic Acid.

$C \times 10^4$.	Λ.	$K \times 10^5$.	$C \times 10^4$.	Λ.	$K \times 10^5$.	$C \times 10^4$.	Λ.	$K \times 10^5$.
9·483	316·75	342	10·427	310·83	340	13·709	297·36	343
7·520	327·31	342	7·925	323·92	342	10·166	312·82	343
5·796	337·71	342	6·104	334·65	341	7·610	326·18	343
4·488	346·77	343	4·578	344·46	337	5·891	336·57	344
3·182	356·65	341	3·562	352·00	335	4·281	347·61	344
0	388·7	—	2·712	359·46	342	3·232	355·27	340
			1·972	366·22	346	2·346	362·99	343
			0	387·5	—	1·717	368·83	344
						0	387·8	—

β-Cyanopropionic acid: Λ_0, 381·1, 380·6. γ-Cyano-*n*-butyric acid: Λ_0, 377·7, 378·1. Dimethylcyanoacetic acid: Λ_0, 380·9, 381·6. *cyclo*Hexylcyanoacetic acid: Λ_0, 371·3, 370·7. *trans*-1-Cyano*cyclo*hexane-2-carboxylic acid: Λ_0, 375·9, 375·3.

Preparation of Materials.—Cyanoacetic acid. Prepared by Phelps and Tillotson's method (*Amer. J. Sci.*, 1908, **26**, 275) and repeatedly crystallised from sodium-dried benzene and light petroleum; m. p. 68—68·5° (Letch and Linstead, J., 1932, 450, give 68°) (Found: C, 42·3; H, 3·4. Calc. for $C_2H_3O_2N$: C, 42·4; H, 3·5%).

β-Cyanopropionic acid. Treatment of sodium β-chloropropionate with potassium cyanide in aqueous solution yielded only succinamic acid (m. p. 153—154°). The cyano-ester was therefore prepared by heating β-chloropropionic ester (25 g.) with potassium cyanide (20 g.) in alcohol (100 c.c.) on the steam-bath for 6 hours. Working up by the usual methods gave 18·5 g. of vacuum-distilled product, b. p. 104—106°/11 mm., $d_4^{20°}$ 1·0359, $n_D^{20°}$ 1·4233 (Found: C, 56·35; H, 7·1. Calc. for $C_6H_9O_2N$: C, 57·0; H, 7·1%). The ester (25 g.) was hydrolysed by 3 days' standing at room temperature with potassium hydroxide (20 g.) in methanol (200 c.c.). The potassium salt was isolated, washed with dry ether, and decomposed in dry benzene by saturation with dry hydrogen chloride (mechanical stirring). Potassium chloride was removed, the benzene evaporated under reduced pressure, and the resulting β-cyanopropionic acid repeatedly crystallised from dry chloroform and light petroleum; m. p. 50—51° (Dakin, *Biochem. J.*, 1917, **11**, 84, gives 48—50°) (Found: C, 48·2; H, 5·2. Calc. for $C_4H_5O_2N$: C, 48·5; H, 5·05%). The presence of water led to hydrolysis of the cyano-ester to succinic acid.

γ-Cyano-n-butyric acid. Vinylacetic acid (Linstead, Noble, and Boorman, J., 1933, 560) was treated with dry hydrogen bromide in 4 vols. of dry toluene (Boorman, Linstead, and Rydon, J., 1933, 573), giving an almost theoretical yield of γ-bromo-*n*-butyric acid, m. p. 32°. This acid was esterified (Wohlgemuth, *Ann. Chim.*, 1914, **2**, 298), and the ester (55 g.), b. p. 88—90°/14 mm., dissolved in alcohol (300 c.c.) and refluxed with potassium cyanide (27 g.) for 48 hours. The product was worked up in the manner already described, and ethyl γ-cyanobutyrate (32 g.) obtained by vacuum distillation, b. p. 120—122°/18 mm. Hydrolysis, by standing with 50% excess of methyl-alcoholic potash at room temperature, yielded, by the usual procedure, γ-cyano-*n*-butyric acid (10 g.), which was recrystallised several times from benzene–light petroleum; m. p. 52—53° (Dieckmann, *Ber.*, 1900, **33**, 588, gives m. p. *ca.* 45°) (Found: C, 53·0; H, 6·3. Calc. for $C_5H_7O_2N$: C, 53·1; H, 6·2%).

Dimethylcyanoacetic acid. The corresponding ester, prepared from sodiocyanoacetic ester and methyl iodide (Hessler, *J. Amer. Chem. Soc.*, 1913, **35**, 990), was purified from monomethyl ester by partial hydrolysis with dilute aqueous sodium hydroxide and vacuum distilled; b. p. 58—60°/1·5—2 mm. (Found: C, 59·4; H, 7·8. Calc. for $C_7H_{11}O_2N$: C, 59·5; H, 7·8%). Hydrolysis with methyl-alcoholic potash and purification in the usual manner yielded dimethylcyanoacetic acid, m. p. 60—61° (Hessler, *J. Amer. Chem. Soc., loc. cit.*, gives 57°; Böhm, *Monatsh.*, 1906, **27**, 952, gives 56—57°) (Found: C, 52·95; H, 6·4. Calc. for $C_5H_7O_2N$: C, 53·1; H, 6·2%).

*cyclo*Hexylcyanoacetic acid. *cyclo*Hexylidenecyanoacetic ester, b. p. 153°/15 mm. (Haworth, Harding, and Perkin, J., 1908, **93**, 1943), was reduced in ethereal solution with aluminium amalgam (Vogel, J., 1927, 597), yielding *cyclo*hexylcyanoacetic ester, b. p. 156°/12 mm., which was hydrolysed at room temperature with methyl-alcoholic potash. The acid was repeatedly recrystallised from benzene–light petroleum; m. p. 81—82° (Found: C, 64·6; H, 7·8. Calc. for $C_9H_{13}O_2N$: C, 64·7; H, 7·8%).

The hexahydrophthalic acids and their half-nitriles. The preparation of *cis*- and *trans*-1-cyano*cyclo*hexane-2-carboxylic acids involved the production of the corresponding hexahydrophthalic acids. The following series of reactions was explored.

(1) Ethyl 1-bromo*cyclo*hexane-2-carboxylate, b. p. 132—136°/14 mm., prepared from *cyclo*hexanone cyanohydrin via Δ^1-tetrahydrobenzonitrile and addition of hydrogen bromide to Δ^1-tetrahydrobenzoic acid, merely lost hydrogen bromide on treatment with potassium cyanide.

(2) 1 : 2-Dibromo*cyclo*hexane, b. p. 105°/20 mm., could not be converted into the dinitrile with potassium or cuprous cyanide under any conditions, including heating in a sealed tube at 200°.

(3) Ethyl *cyclo*hexanone-2-carboxylate (Kotz, *Annalen*, 1906, **350**, 210; 1908, **358**, 198) was converted into the *cyanohydrin*, b. p. 168—170°/30 mm., m. p. 53—54°, $d_4^{25°}$ 1·1053, $n_D^{25°}$ 1·4637 (supercooled liquid in each case) (Found: C, 61·0; H, 7·8. $C_{10}H_{15}O_3N$ requires C, 60·9; H, 7·6%), and this, in turn, into *ethyl* 1-*cyano*cyclo*hexene-2-carboxylate*, b. p. 149—151°/8 mm.; $d_4^{25°}$ 1·0677, $n_D^{25°}$ 1·4843 (Found: C, 66·7; H, 7·1. $C_{10}H_{13}O_2N$ requires C, 67·0; H, 7·3%), but this could not be reduced either by hydrogenation in the presence of Adams's catalyst or by aluminium amalgam.

(4) Δ^1-Tetrahydrobenzonitrile (22 g.), potassium cyanide (53 g.), alcohol (200 c.c.), water (100 c.c.), and concentrated hydrochloric acid (20 c.c.) were heated in a pressure bottle at 100° for 4 hours. After cooling, the alcohol was removed, and the solution extracted with ether, the aqueous layer being set aside. The extract, washed with concentrated calcium chloride solution and dried, yielded 1 : 2-*dicyano*cyclo*hexane* (10 g.), b. p. 184—188°/25 mm., m. p. 42° (Found : C, 71·2; H, 7·6. $C_8H_{10}N_2$ requires C, 71·5; H, 7·6%), hydrolysed to *trans*-hexahydrophthalic acid, m. p. and mixed m. p. 220°. The aqueous layer, on acidification, removal of hydrogen cyanide, and ether extraction, gave a small amount of *cis*-hexahydrophthalic acid, m. p. and mixed m. p. 189°.

trans-*Hexahydrophthaloyl chloride* (20 g.), b. p. 145—146°/20 mm. (Found : Cl, 33·9. $C_8H_{10}O_2Cl_2$ requires Cl, 34·0%), prepared by heating the acid with phosphorus pentachloride, was slowly added to ammonia (*d* 0·88; 200 c.c.); a vigorous reaction ensued and the mixture was left overnight. Excess ammonia was removed, and the solution concentrated under reduced pressure. Acidification and ether extraction, followed by working up in the usual way, provided trans-1-*cyano*cyclo*hexane*-2-*carboxylic acid* (10 g.), which was crystallised from aqueous alcohol; m. p. 128—129° (Found : C, 62·7; H, 7·3; equiv., by titration, 153. $C_8H_{11}O_2N$ requires C, 62·7; H, 7·2%; equiv., 153). Acid or alkaline hydrolysis yielded *trans*-hexahydrophthalic acid.

Similar treatment of *cis*-hexahydrophthalic acid afforded, not the *cis*-, but the *trans*-dichloride [identity of b. p., production of same *trans*-dianilide (m. p. and mixed m. p. 301°), and of same cyano-acid as the above on treatment with ammonia]. Treatment of the *cis*-acid in ethereal solution with phosphorus pentachloride gave the *cis*-acid chloride. This could not be isolated by distillation, but its production was demonstrated by formation of the *cis*-anilide, m. p. 234° after recrystallisation from dilute acetic acid, and thence of the phenylimide, m. p. 130°, by refluxing for several hours with 80% acetic acid. Stoermer and Steinbeck (*Ber.*, 1932, **65**, 417) give m. p.'s 234° and 132°, respectively, and state that 80% acetic acid has no action on the *trans*-dianilide. The action of ammonia (*d* 0·88) on the *cis*-chloride yielded only *cis*-hexahydrophthalamic acid, m. p. 168—170°. Use of thionyl chloride instead of phosphorus pentachloride led to the same result.

(5) Ethyl *cyclo*hexanone-2-carboxylate cyanohydrin (10 g.) in the minimum of benzene was slowly added to phosphorus pentachloride (11 g.), cooled in ice. After 2 hours, the mixture was poured into water and extracted with ether. The extract, on being worked up in the usual manner, yielded *ethyl* 1-*chloro*-1-*cyano*cyclo*hexane*-2-*carboxylate*, which crystallised from aqueous alcohol in fine silky needles, m. p. 87—88° (Found : Cl, 17·2. $C_{10}H_{14}O_2NCl$ requires Cl, 17·5%). This ester (5 g.) in 50% acetic acid (50 g.) was treated slowly (4—5 hrs.) with zinc dust (2·5 g.), and left on the steam-bath overnight. Working up in the usual manner afforded ethyl *trans*-1-cyano*cyclo*hexane-2-carboxylate (3 g.), b. p. 140°/9 mm., hydrolysed to *trans*-hexahydrophthalic acid, m. p. and mixed m. p. 218°, but as this ester was impure and the yield small, the cyano-acid for the conductivity measurements was obtained by method (4).

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137. *The Elimination of Chlorine from Sodium Chloroacetate by the Salts of Weak Acids.*

By (the late) H. M. DAWSON, E. R. PYCOCK, and GILBERT F. SMITH.

The elimination of chlorine from the chloroacetate ion is brought about by water and by basic anions. The reactivity of 34 anions has been examined, and the bimolecular velocity coefficients measured at 45° in solutions of unit ionic strength. The velocity coefficient increases with the basic strength of the participating base.

IN previous papers (J., 1933, 49, 1133; 1934, 778; 1936, 153, 487; *Proc. Leeds Phil. Soc.*, 1934, **2**, 544; 1935, **3**, 135, 293) kinetic measurements on the removal of halogen from the $CH_2X{\cdot}CO_2^-$ group (X = Cl or Br) in neutral, acid, and alkaline solutions were reported. By restricting the measurements of velocity to the very early stages of the reaction, complications arising from the intervention of reaction products are largely avoided, and in these circumstances it was found that the velocity of reaction could be represented as the sum of five independent processes, as follows :

$$(1)\ CH_2X{\cdot}CO_2^- + H_2O \longrightarrow CH_2(OH){\cdot}CO_2H + X^-$$

$$(2)\ CH_2X{\cdot}CO_2^- + OH^- \longrightarrow CH_2(OH){\cdot}CO_2^- + X^-$$

$$(3)\ CH_2X{\cdot}CO_2^- + CH_2X{\cdot}CO_2^- \longrightarrow CH_2X{\cdot}CO_2CH_2{\cdot}CO_2^- + X^-$$

$$(4)\ CH_2X{\cdot}CO_2^- + CH_2X{\cdot}CO_2H \longrightarrow CH_2X{\cdot}CO_2CH_2{\cdot}CO_2H + X^-$$

$$(5)\ CH_2X{\cdot}CO_2H + H_2O \longrightarrow CH_2(OH){\cdot}CO_2H + H^+ + X^-$$

If attention is confined to alkaline or neutral solutions containing initially the salt $CH_2X{\cdot}CO_2Na$, then in the virtual absence of the acid $CH_2X{\cdot}CO_2H$, account need be taken of reactions (1)—(3) only. Each of these reactions involves the interaction of the ion $CH_2X{\cdot}CO_2^-$ with a substance which on present views is a base, and it might therefore be anticipated that these are but special cases of a general reaction involving $CH_2X{\cdot}CO_2^-$ and any base of sufficient strength. Evidence for this view has already been given in the case of sodium

bromoacetate, where it was shown that the weakly basic anions chloroacetate, glycollate, formate, and acetate all undergo reaction in accord with the general equation

$$(6)\ CH_2X\cdot CO_2^- + B^- \longrightarrow CH_2B\cdot CO_2^- + X^-$$

where B^- stands for the basic anion.

TABLE I.

Initial velocities for 0·2M-$CH_2Cl\cdot CO_2Na$ + xM-NaB + (0·8 − x)M-$NaNO_3$ *at* 45°.

B^- = Formate; 10^6k_6 = 20·3.

x	0	0·0791	0·10	0·158	0·237	0·30	0·316	0·396	0·50
$10^6V_{obs.}$	0·560	0·864	0·958	1·19	1·53	1·78	1·84	2·18	2·61
$10^6V_{calc.}$	0·558	0·879	0·965	1·20	1·52	1·78	1·84	2·17	2·59

B^- = Acetate; 10^6k_6 = 15·5.

x	0	0·10	0·20	0·30	0·40	0·50
$10^6V_{obs.}$	0·562	0·857	1·16	1·44	1·82	2·15
$10^6V_{calc.}$	0·558	0·868	1·18	1·49	1·80	2·11

B^- = Propionate; 10^6k_6 = 15·0.

x	0	0·10	0·30	0·50
$10^6V_{obs.}$	0·561	0·842	1·46	2·08
$10^6V_{calc.}$	0·558	0·858	1·46	2·06

B^- = *n*-Butyrate; 10^6k_6 = 13·8.

x	0	0·10	0·20	0·30
$10^6V_{obs.}$	0·557	0·820	1·12	1·41
$10^6V_{calc.}$	0·558	0·834	1·11	1·39

B^- = Glycollate; 10^6k_6 = 10·8.

x	0	0·10	0·20	0·30	0·40
$10^6V_{obs.}$	0·560	0·777	0·984	1·20	1·43
$10^6V_{calc.}$	0·558	0·775	0·990	1·21	1·43

B^- = Phenylacetate; 10^6k_6 = 11·6.

x	0	0·099	0·198	0·297
$10^6V_{obs.}$	0·560	0·788	1·02	1·25
$10^6V_{calc.}$	0·558	0·788	1·02	1·25

B^- = Phenylpropionate; 10^6k_6 = 13·3.

x	0	0·1	0·2	0·3
$10^6V_{obs.}$	0·560	0·821	1·09	1·37
$10^6V_{calc.}$	0·558	0·824	1·09	1·36

B^- = *p*-Nitrophenylacetate; 10^6k_6 = 9·8.

x	0	0·05	0·1	0·2
$10^6V_{obs.}$	0·556	0·649	0·760	0·966
$10^6V_{calc.}$	0·558	0·656	0·754	0·952

B^- = Benzoate; 10^6k_6 = 9·5.

x	0	0·1	0·3	0·5
$10^6V_{obs.}$	0·557	0·740	1·11	1·52
$10^6V_{calc.}$	0·558	0·748	1·13	1·51

B^- = Mandelate; 10^6k_6 = 8·2.

x	0	0·1	0·2	0·3
$10^6V_{obs.}$	0·561	0·715	0·893	1·07
$10^6V_{calc.}$	0·558	0·722	0·886	1·05

B^- = *o*-Toluate; 10^6k_6 = 12·3.

x	0	0·1	0·2	0·3
$10^6V_{obs.}$	0·560	0·802	1·04	1·30
$10^6V_{calc.}$	0·558	0·804	1·05	1·30

B^- = *m*-Toluate; 10^6k_6 = 9·8.

x	0	0·1	0·2	0·3
$10^6V_{obs.}$	0·557	0·750	0·947	1·16
$10^6V_{calc.}$	0·558	0·754	0·950	1·15

B^- = *p*-Toluate; 10^6k_6 = 10·2.

x	0	0·1	0·2	0·3
$10^6V_{obs.}$	0·561	0·757	0·963	1·18
$10^6V_{calc.}$	0·558	0·764	0·968	1·17

B^- = *o*-Hydroxybenzoate; 10^6k_6 = 4·4.

x	0	0·1	0·2	0·3
$10^6V_{obs.}$	0·557	0·648	0·737	0·831
$10^6V_{calc.}$	0·558	0·648	0·736	0·824

B^- = *m*-Hydroxybenzoate; 10^6k_6 = 11·1.

x	0	0·1	0·2	0·3
$10^6V_{obs.}$	0·560	0·780	1·02	1·21
$10^6V_{calc.}$	0·558	0·780	1·00	1·21

B^- = *p*-Hydroxybenzoate; 10^6k_6 = 12·6.

x	0	0·1	0·2	0·3
$10^6V_{obs.}$	0·556	0·818	1·06	1·31
$10^6V_{calc.}$	0·558	0·812	1·06	1·32

B^- = *o*-Nitrobenzoate; 10^6k_6 = 4·5.

x	0	0·1	0·2	0·3
$10^6V_{obs.}$	0·561	0·643	0·740	0·837
$10^6V_{calc.}$	0·558	0·648	0·738	0·828

B^- = *m*-Nitrobenzoate; 10^6k_6 = 6·6.

x	0	0·1	0·2	0·3
$10^6V_{obs.}$	0·563	0·692	0·823	0·966
$10^6V_{calc.}$	0·558	0·690	0·822	0·954

B^- = *p*-Nitrobenzoate; 10^6k_6 = 7·3.

x	0	0·1	0·2	0·3
$10^6V_{obs.}$	0·557	0·704	0·859	1·00
$10^6V_{calc.}$	0·558	0·706	0·852	0·998

B^- = *o*-Chlorobenzoate; 10^6k_6 = 6·1.

x	0	0·1	0·2	0·3
$10^6V_{obs.}$	0·560	0·681	0·821	0·924
$10^6V_{calc.}$	0·558	0·682	0·805	0·926

B^- = *m*-Chlorobenzoate; 10^6k_6 = 8·2.

x	0	0·1	0·2	0·3
$10^6V_{obs.}$	0·556	0·718	0·897	1·06
$10^6V_{calc.}$	0·558	0·722	0·886	1·05

B^- = *p*-Bromobenzoate; 10^6k_6 = 9·3.

x	0	0·1	0·15	0·2
$10^6V_{obs.}$	0·560	0·747	0·839	0·929
$10^6V_{calc.}$	0·558	0·746	0·839	0·933

B^- = *p*-Chlorobenzoate; 10^6k_6 = 8·7.

x	0	0·1	0·2	0·3	0·4
$10^6V_{obs.}$	0·563	0·729	0·905	1·09	1·26
$10^6V_{calc.}$	0·558	0·734	0·908	1·08	1·26

The experiments to be described show that analogous processes are effective in the elimination of chlorine from $CH_2Cl{\cdot}CO_2^-$. The evidence for this is provided chiefly by measurements at 45° of the initial velocities in aqueous solutions containing sodium chloroacetate and the sodium salts of various weak acids under controlled conditions of total salt concentration. Under the experimental conditions reaction (2) may be neglected, and the reaction velocity will be given by the equation

$$V_{obs.} = V_1 + V_3 + V_6 = k_1[A^-] + k_3[A^-]^2 + k_6[A^-][B^-] \quad . \quad . \quad . \quad . \quad . \quad . \quad (a)$$

where V_6 and k_6 relate to reaction (6) and $[A^-]$ and $[B^-]$ represent respectively the concentration of chloroacetate and the basic anion. Measurement of the initial rate of production of chloride, together with a knowledge of k_1 and k_3, allows of the evaluation of k_6. In this paper the same units are employed as in the previous papers of the series; time is given in minutes, and concentration in g.-mols./l.

A. *Salts of Monocarboxylic Acids.*—The reaction mixtures were of compositions given by the general formula $0{\cdot}2$M-$CH_2Cl{\cdot}CO_2Na$ + xM-NaB + $(0{\cdot}8 - x)$M-$NaNO_3$. Since the salts involved are uni-univalent, the ionic strength of the solutions is unity and hence, provided specific salt effects be negligible, no differential inert-salt effect should occur on varying x. In Table I are given the kinetic data for the salts of aliphatic and aromatic acids. The values of $V_{calc.}$ are in each case those obtained by means of equation (a), the values of k_6 being those given in the table, and it being assumed that $10^6k_1 = 1{\cdot}65$ and $10^6k_3 = 5{\cdot}7$. The close agreement obtained in each case between observed and calculated velocities indicates that the inert-salt effects due to the nitrate and the basic anions cannot differ to any marked extent.

B. *Salts of Polycarboxylic Acids.*—The reaction mixtures had the composition $0{\cdot}2$M-$CH_2Cl{\cdot}CO_2Na$ + xM-Na_zB + $(0{\cdot}8 - zx)$M-$NaNO_3$, where z is the valency of the anion derived from the salt Na_zB. In such a series of solutions the change in ionic strength with variation of x may bring about corresponding changes in the various velocity coefficients, and account must be taken of this in order to evaluate k_6 under salt conditions comparable to those obtaining in section A ($\mu = 1$). Examination of the experimental material shows that for all the solutions the observed velocities are closely accounted for by equation (a) on taking constant values for the coefficients k_1 and k_3, and by assuming that the value of the coefficient k_6 is related to the ionic strength by the empirical equation

$$\log k_6' = \log k_6 + \alpha(\mu - 1) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (b)$$

where k_6' and k_6 refer respectively to ionic strengths of μ and of unity, and α is a constant specific to the salt Na_zB. This is shown by the data in Table II, which relate to the reaction between malonate and chloroacetate ions. The values of $V_{calc.}$ given in the last line are obtained by means of equations (a) and (b), the various constants being assigned the values $10^6k_1 = 1{\cdot}65$; $10^6k_3 = 5{\cdot}7$; $10^6k_6 = 31{\cdot}1$; $\alpha = 0{\cdot}200$.

TABLE II.

Initial velocities for $0{\cdot}2$M-$CH_2Cl{\cdot}CO_2Na$ + xM-$CH_2(CO_2Na)_2$ + $(0{\cdot}8 - 2x)$M-$NaNO_3$ *at* 45°.

x	0	0·05	0·10	0·15	0·20	0·30
μ	1·0	1·05	1·1	1·15	1·2	1·3
$10^6V_{obs.}$	0·557	0·870	1·20	1·51	1·89	2·66
$10^6V_{calc.}$	0·558	0·875	1·21	1·56	1·92	2·70

The method described above for the evaluation of the limiting value of $k_6(\mu = 1)$ will be valid provided that, as μ increases, the contributions to the total velocity made by V_1 and V_3 progressively decrease to an appropriate extent. Inspection of numbers in Table II shows that this condition is likely to obtain; *e.g.*, when $x = 0{\cdot}30$ and $\mu = 1{\cdot}3$, then V_1 and V_3 together account for only about 21% of the total velocity, so that considerable uncertainty as to the precise magnitudes of V_1 and V_3 can no longer be of importance.

The results given above are typical of those obtained for this group of anions, and the remainder of the observations are therefore given in summarised form. In cols. 2 and 3 of Table III are given respectively the range of x values employed and the values of α in equation (b), and in col. 4 are the values for $k_6(\mu = 1)$ derived by means of (a) and (b).

TABLE III.

Reactant.	x.	α.	10^6k_6.	Reactant.	x.	α.	10^6k_6.
Oxalate	0—0·15	0·210	26·4	Malate	0—0·40	0·130	26·3
Malonate	0—0·30	0·200	31·1	Tartrate	0—0·30	0·140	21·3
Succinate	0—0·30	0·147	29·9	Phthalate	0—0·15	0	31·8
Adipate	0—0·15	0·135	26·3	Citrate	0—0·25	0	55

C. *Sodium Carbonate.*—The experimental procedure described in sections A and B is no longer applicable when the basic reactant is derived from sodium carbonate, since the hydrolysis of this salt is by no means negligible in dilute aqueous solution. It is therefore necessary to repress the hydrolysis by the addition of free alkali. Measurements of initial velocity were made for mixtures of the type aM-$CH_2Cl{\cdot}CO_2Na$ + bN-NaOH + cM-Na_2CO_3 + $(1 - a - b - 2c)$M-$NaNO_3$, where a and b had values 0·2 and 0·01 respectively, and c ranged from 0·1 to 0·3. If x is the concentration of chloride ions at time t, then the rate of reaction is given by

$$dx/dt = k_1[A^-] + k_3[A^-]^2 + k_6[A^-][CO_3^{--}] + k_2[A^-][OH^-]$$

Now in the presence of free alkali the production of acid keeps pace with the production of halogen, since the compounds formed by reactions (3) and (6) undergo very rapid hydrolysis thus :

$$(6a)\quad CH_2B{\cdot}\bar{C}O_2 + H_2O \longrightarrow CH_2(OH){\cdot}\bar{C}O_2 + HB$$

Hence the above velocity equation may be written

$$dx/dt = k_1a + k_3a^2 + k_6ac + k_2a(b - x)$$

or

$$dx/dt = m + k_2a(b - x)$$

where $m = k_1a + k_3a^2 + k_6ac$. Integration of this equation, m being treated as a constant, gives

$$e^{tk_2a} = (m + k_2ab)/[m + k_2a(b - x)]$$

Consequently, if x_0 and x refer respectively to times t_0 and t, then

$$e^{(t - t_0)k_2a} = [m + k_2a(b - x_0)]/[m + k_2a(b - x)]$$

which gives

$$m = k_2a\left[\frac{xe^{(t - t_0)k_2a} - x_0}{e^{(t - t_0)k_2a} - 1} - b\right] = k_1a + k_3a^2 + k_6ac$$

whence

$$k_6 = k_2\left[\frac{xe^{(t - t_0)k_2a} - x_0}{e^{(t - t_0)k_2a} - 1} - b\right] - k_1 - k_3a/c \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (c)$$

The experimental results are in Table IV, where t_0 relates to the first titration in each experiment and x_0 is the value of x when $t - t_0 = 0$. The values of k_6 have been calculated from (*c*) with the previous values for k_1 and k_3 and with $10^6k_2 = 1040$ (for the evaluation of k_1, k_2, and k_3, see papers cited on p. 517).

TABLE IV.

Initial velocities for 0·2M-$CH_2Cl{\cdot}CO_2Na$ + 0·01M-NaOH + *c*M-Na_2CO_3 + (0·79 − *c*)M-$NaNO_3$ at 45°.

	c = 0·100.				c = 0·200.				c = 0·300.			
$t - t_0$	0	800	820	841	0	506	522	555	0	410	433	462
10^3x	0·140	4·152	4·251	4·361	0·279	4·251	4·391	4·591	0·359	4·900	5·140	5·389
10^6k_6	—	142	142	143	—	142	145	142	—	150	150	147

The change in the value of k_6 with increase in c is little more than the possible experimental error, and is in all probability due to the change in ionic strength from 1·1 (c = 0·1) to 1·3 (c = 0·3). The value adopted for $10^6k_6(\mu = 1)$ is 140 and is considered to be substantially correct.

For purpose of comparison the velocity coefficients referred to in the preceding pages are collected together in the following table. It is not proposed yet to discuss the implications of these results, but it may be remarked that consideration of the values of 10^6k_6 for water (1·65) and for the ions acetate (15·5), carbonate (140), hydroxyl (1040), indicates clearly that there exists a general relation connecting velocity coefficient and the basic strength of the participating base.

Velocity coefficients (k_6) *for the reaction between chloroacetate ions and bases at* 45°.

Base.	10^6k_6.	Base.	10^6k_6.	Base.	10^6k_6.
Water	1·65	*Univalent anions.*		*Univalent anions.*	
Bi- and ter-valent anions.		Formate	20·3	*m*-Toluate	9·8
Oxalate	26·4	Acetate	15·5	*p*-Toluate	10·2
Malonate	31·1	Propionate	15·0	*o*-Hydroxybenzoate	4·4
Succinate	29·6	Butyrate	13·8	*m*-Hydroxybenzoate	11·1
Adipate	26·3	Chloroacetate	5·7	*p*-Hydroxybenzoate	12·6
Malate	26·2	Glycollate	10·8	*o*-Nitrobenzoate	4·5
Tartrate	21·3	Phenylacetate	11·6	*m*-Nitrobenzoate	6·6
Phthalate	31·8	Phenylpropionate	13·3	*p*-Nitrobenzoate	7·3
Carbonate	140	*p*-Nitrophenylacetate	9·8	*o*-Chlorobenzoate	6·1
Citrate	55	Benzoate	9·5	*m*-Chlorobenzoate	8·2
		Mandelate	8·2	*p*-Chlorobenzoate	8·7
		o-Toluate	12·3	*p*-Bromobenzoate	9·3
				Hydroxyl	1040

EXPERIMENTAL.

The general procedure was as described in previous papers. The estimation of chloride was by Drechsel's method (*Z. anal. Chem.*, 1877, **16**, 351). The sample of reaction mixture was run into a measured volume of N/20-silver nitrate containing sufficient nitric acid to coagulate the silver chloride. This was filtered off, washed thoroughly, and the filtrate titrated with thiocyanate. In general, the accuracy of the method appears to be unimpaired by the presence of the organic acids which are liberated by the nitric acid from the corresponding salts. When, however, the organic acid is only sparingly soluble in water, it is necessary first to precipitate the acid by addition of nitric acid, followed by extraction with ether or benzene, before proceeding to the chloride estimation.

In the presence of oxalic acid Drechsel's method is not applicable, since this acid reacts with the ferric indicator, and Liebig's method of estimation (*Annalen*, 1851, **77**, 102) was adopted. The sample containing sodium oxalate was added to excess silver nitrate solution and the precipitated silver chloride filtered off, well washed, and then dissolved in ammonia. To the resulting solution was added slight excess of N/20-potassium cyanide, followed by 5 c.c. of 2% potassium iodide solution. This liquid was then titrated against N/100-silver nitrate until a permanent turbidity was produced on stirring.

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138. *The Brönsted Relation in the Hydrolysis of the Halogenoacetates and the Theory of Acids and Bases.*

By Gilbert F. Smith.

The hydrolysis of the chloroacetate ion is subject to general basic catalysis, and the Brönsted catalysis relation is found to hold for a series of basic catalysts, although important exceptions are noted.
The bearing of these results on the theory of acids and bases is discussed.

The hydrolysis of the group $CH_2X{\cdot}\bar{C}O_2$ (X = Cl or Br) is represented by the stoicheiometric equation $CH_2X{\cdot}\bar{C}O_2 + H_2O \longrightarrow CH_2(OH){\cdot}CO_2H + \bar{X}$, but the actual mechanism by which the reaction products are formed is complex and consists primarily of a series of simultaneous bimolecular reactions involving the $CH_2X{\cdot}\bar{C}O_2$ ion and each basic species present. Except in the direct reaction in which water molecules participate, these simultaneous reactions can be written as

$$CH_2X{\cdot}\bar{C}O_2 + \bar{B} \longrightarrow CH_2B{\cdot}\bar{C}O_2 + \bar{X} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where B is a base which may thus be the hydroxyl ion, the chloroacetate ion, or any basic anion present in the solution. Except when $\bar{B}$ is the hydroxyl ion, the product formed in (1) is then hydrolysed by the solvent in accord with the equation

$$CH_2B{\cdot}\bar{C}O_2 + H_2O \longrightarrow CH_2(OH){\cdot}CO_2H + \bar{B} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Although the rate of reaction (2) is not known, it is clear that the base catalyses the hydrolytic reaction, since it brings about an alteration in the speed of the reaction and is itself eventually re-formed. Moreover, since a variety of bases are effective (Dawson, Pycock, and Smith, preceding paper) the reaction is subject to general basic catalysis and it therefore becomes of interest to enquire whether this reaction, like other base-catalysed reactions, conforms to the Brönsted catalysis relation. For basic catalysis this relation may be written in the form $\log (k/q) = \log G + \beta \log (K_b p/q)$, where k is the velocity coefficient of reaction (1), K_b is the basic dissociation constant of $\bar{B}$, G and β are constants for a given temperature, and p and q are statistical factors. The relevant data are recorded in Tables I and II, which refer respectively to the hydrolysis of the chloro- and the bromo-acetate group. In the former case, since the velocity coefficients refer to 45°, values for K_b are used at or near this temperature when these data are available, but otherwise those at 25°. Except with the very strong bases, however, the exact temperature to which K_b refers (col. 3) is not of great significance. All the velocity coefficients, except that for the sulphite ion, relate to solutions in which the ionic strength was unity, whereas the dissociation constants refer to dilute, and in some cases to infinitely dilute, solutions; but no difficulty arises in respect of this, since it is probable (Dawson and Lowson, J., 1929, 1217) that the dissociation constants of different acids vary with the ionic strength of the solution in a precisely similar manner.

Inspection of the numbers in the body of Table I shows that the equation at the head of the table accounts satisfactorily for the experimental values of k, except in the case of water, where the reaction is somewhat different. The data in Table II show that for the hydrolysis of the bromoacetate group a relation of the same type probably exists, with a very similar value for β. At the foot of the tables are also given the velocity coefficients for the sulphite and the thiosulphate ion (Krapavin, *J. Chim. physique*, 1912, **10**, 289; La Mer, *Chem. Rev.*, 1932, **10**, 179). It is obvious that the relation breaks down completely for these ions, and that here specific effects have a preponderating influence. Although specific effects of these very large magnitudes have not previously been observed, it is well established that they do occur in lesser degree in other base-catalysed reactions, *e.g.*, in the nitroamide reaction and the mutarotation of glucose (see Hammet, "Physical Organic Chemistry," McGraw-Hill Book Co., 1940, p. 225; Bell, "Acid–Base Catalysis," Clarendon Press, 1941, p. 88), so the difference between the two classes of reaction would appear to be one of degree rather than of kind.

The results given above lead unquestionably to the conclusion that the basic catalysis of the hydrolysis of the group $CH_2X{\cdot}\bar{C}O_2$ exhibits, in the main, the characteristics usually associated with general acid–base catalysis. On the basis of present views this is surprising, since there appears to be an important difference in reaction type. It is generally accepted that acid–base catalysed reactions are protolytic processes. For instance, in the conversion of the species SH into products X under the catalytic influence of a base $\bar{B}$, the rate-determining step can be formulated as $SH + \bar{B} \longrightarrow \bar{S} + HB$, and this is followed by rapid reactions involving the conversion of $\bar{S}$ into X and the regeneration of $\bar{B}$. In the present case, no proton transfer can be involved, the primary reaction being the displacement of $\bar{X}$ by $\bar{B}$ from the group $CH_2X{\cdot}\bar{C}O_2$, in accord with equation (1). It can only be concluded, therefore, that the transfer of a proton is not, as usually supposed, an essential process in basic or acid catalysis. If this is accepted, then, since acid–base catalysis must involve

the acid and basic functions of the species concerned, it follows that in acid–base equilibria the proton is not, of necessity, involved.

TABLE I.

The Brönsted relation in the reaction $CH_2Cl\cdot\bar{C}O_2 + \bar{B} \longrightarrow CH_2B\cdot\bar{C}O_2 + \bar{C}l$ (45°).

$\log(k/q) = -6{\cdot}090 + 0{\cdot}203 \log(K_b p/q)$.

No.	Base.	log K_b.	Temp.	p.	q.	10^6k, calc.	10^6k, obs.
1	Water	−1·74	45°	1	1	(0·36)	0·030
2	*o*-Nitrobenzoate	2·17	25	1	2	3·9	4·4
3	*o*-Hydroxybenzoate	2·98	25	1	2	5·7	4·5
4	Chloroacetate	2·91	45	1	2	5·5	5·7
5	*o*-Chlorobenzoate	2·94	25	1	2	5·6	6·1
6	*m*-Nitrobenzoate	3·46	50	1	2	7·1	6·5
7	*p*-Nitrobenzoate	3·42	25	1	2	6·9	7·3
8	Mandelate	4·37	25	1	2	10·9	8·2
9	*m*-Chlorobenzoate	3·83	25	1	2	8·5	8·2
10	*p*-Chlorobenzoate	3·98	25	1	2	9·1	8·7
11	*p*-Bromobenzoate	3·97	25	1	2	9·1	9·3
12	Benzoate	4·18	45	1	2	10·0	9·5
13	*p*-Nitrophenylacetate	4·85	25	1	2	13·7	9·8
14	*m*-Toluate	4·17	25	1	2	9·9	9·8
15	*p*-Toluate	4·62	25	1	2	12·2	10·6
16	Glycollate	3·84	45	1	2	8·5	10·8
17	*m*-Hydroxybenzoate	4·08	25	1	2	9·5	11·1
18	Phenylacetate	4·29	35	1	2	10·5	11·6
19	*o*-Toluate	3·91	25	1	2	10·1	12·3
20	*p*-Hydroxybenzoate	4·54	25	1	2	11·8	12·6
21	*n*-Butyrate	4·87	45	1	2	13·8	13·8
22	Propionate	4·90	45	1	2	14·0	15·0
23	Acetate	4·78	45	1	2	10·3	15·5
24	Formate	3·77	45	1	2	8·3	20·3
25	Tartrate	4·54	25	1	4	20·5	21·3
26	Malate	5·13	25	1	4	27·7	26·3
27	Oxalate	4·39	45	1	4	24·0	26·4
28	Succinate	5·7	37—50	1	4	34·9	29·9
29	Malonate	5·36	25	1	4	30·1	31·1
30	Phthalate	5·41	25	1	4	30·8	31·8
31	Carbonate	10·22	38	1	3	230	140
32	Hydroxyl	15·14	45	1	1	960	1040
33	Sulphite	5·3	25	—	—	—	4610 (25°) ($\mu = 0$)
34	Thiosulphate	2	25	—	—	—	10,700 (25°)

TABLE II.

The Brönsted relation in the reaction $CH_2Br\cdot\bar{C}O_2 + \bar{B} \longrightarrow CH_2B\cdot\bar{C}O_2 + \bar{B}r$ *at* 25°.

$\log(k/q) = -5{\cdot}500 + 0{\cdot}198 \log(K_b p/q)$.

No.	Base.	log K_b (25°).	p.	q.	10^6k, calc.	10^6k, obs.
1	Water	−1·74	1	1	(1·43)	0·059
4	Chloroacetate	2·86	1	2	23·3	14·0
35	Bromoacetate	2·86	1	2	23·3	19·3
16	Glycollate	3·83	1	2	31·6	35
24	Formate	3·75	1	2	30·5	50
23	Acetate	4·76	1	2	48·3	50
32	Hydroxyl	15·74	1	1	4140	4150
34	Thiosulphate	2	—	—	—	$1{\cdot}065 \times 10^6$

References to dissociation constants : (4) Wright, *J. Amer. Chem. Soc.*, 1934, **56**, 314 (extrapolated); (16) Nims, *ibid.*, 1936, **58**, 987 (interpolated); (21) Harned and Sutherland, *ibid.*, 1934, **56**, 2039; (22) Harned and Ehlers, *ibid.*, 1933, **55**, 2379; (23) *Idem, ibid.*, p. 652; (24) Harned and Embree, *ibid.*, 1934, **56**, 1042; (27) Harned and Fallon, *ibid.*, 1939, **61**, 3111; (32) Harned and Hamen, *ibid.*, 1933, **55**, 2194; (2), (3), (5), (7), (9), (10), (11), (13), (14), (15), (17), (19), (20) Watson, "Modern Theories of Organic Chemistry," 1937, pp. 36, 207; (6), (8), (12), (18), (25), (26), (28), (29), (30), (31), (33), (34), (35) Landolt–Börnstein, "Tabellen," 1923 and 1931.

References to velocity coefficients : Dawson and Pycock, J., 1934, 778; 1936, 153; Dawson, Pycock, and Smith, *loc. cit.*; Dawson and Dyson, J., 1933, 49; Brook and Dawson, J., 1936, 497.

This is in sharp disagreement with the Lowry–Brönsted definition of acids and bases, which, as summarised by the relation $B + H^+ \rightleftarrows BH^+$, insists that the proton plays a necessary and vital part. Since this is not the case, it becomes necessary to take a broader view, as suggested by Lewis (*J. Franklin Inst.*, 1938, **226**, 293). A base may then be defined as a species possessing a free electron pair which can enter the shell of another atom, and an acid as a species which can receive such an electron pair. These definitions may conveniently be expressed by the scheme $B) +)A \rightleftarrows BA$, where) after the letter represents a free electron pair and) before the letter represents the corresponding deficiency. This concept introduces no new bases, since every base defined in this manner will also be a base on the Lowry–Brönsted view, but it displaces the proton from its unique position in that it recognises the fact that the proton is one only amongst many species, each of which, in virtue of its ability to accept an electron pair, may therefore combine with a base.

Such an extension of our present views is permissible only if it can be demonstrated that acids and bases as defined above conform closely to the generally recognised criteria of acids and bases. In this connection it is noted that Lewis (*loc. cit.*) has recorded a number of experiments involving substances of the type B) and)A, both these and the solvent media being chosen so as to exclude the possibility of protolytic reactions. In these circumstances, he demonstrated that, qualitatively at least, these substances simulate in a very remarkable manner some of the salient properties normally associated with acids and bases. The experiments referred to in the present paper, although of a very different nature, lead to the same conclusion, and receive a ready explanation in terms of the views expressed above. The group $CH_2X{\cdot}\bar{C}O_2$ may be regarded as a compound formed from the base $\bar{X})$ and the acid $)\overset{+}{C}H_2{\cdot}\bar{C}O_2$.* On addition of the stronger base $\bar{B})$, the weak base $\bar{X})$ is displaced from its compound with the acid. This, then, becomes a normal acid–base reaction. Furthermore, on comparing the reactions (3) and (4), a parallelism between them is understand-

$$CH_2X{\cdot}\bar{C}O_2 + \bar{B}) \longrightarrow CH_2B{\cdot}CO_2 + \bar{X}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$\overset{+}{H_3}O + \bar{B}) \rightleftarrows HB + H_2O) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

able only if both are recognised as reactions of essentially the same type, *i.e.*, acid–base reactions.

It should be pointed out that the parallelism between (3) and (4) would be expected to be less pronounced than in those cases where both the reacting systems involve protolytic reactions. For in the processes $SH + \bar{B}) \longrightarrow \bar{S}) + HB$ and $\overset{+}{H_3}O + \bar{B}) \rightleftarrows H_2O) + HB$ the acid $)H^+$ and the base $\bar{B})$ are involved in both, while in (3) and (4) the only common factor is the base $\bar{B})$, and hence specific effects are likely to be of much greater importance in the latter case. Indeed, since, in general, the ability of an acid and base to react is essentially specific in character, it may be regarded as the exception that a relation should exist between the abilities of two acids $)H^+$ and $)\overset{+}{C}H_2{\cdot}\bar{C}O_2$ to react with a series of bases, and it is in no way surprising that in other cases this parallelism should no longer be found.

THE UNIVERSITY, LEEDS.

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139. *The Triterpene Resinols and Related Acids. Part XIV. The Oxidation of Acetylursolic Acid.*

By E. S. EWEN and F. S. SPRING.

Oxidation of acetylursolic acid, $C_{32}H_{50}O_4$, yields ketoacetylursolic acid, $C_{32}H_{48}O_5$ (major product), and a *lactone*, $C_{32}H_{46}O_4$. Ketoacetylursolic acid is shown to be an *αβ*-unsaturated ketone; when heated with quinoline it loses the elements of formic acid to give *nor-α-amyradienonyl acetate*, which contains the chromophoric system O:C·C:C·C:C. These transformations indicate that the carboxyl group of ursolic acid is in the vicinity of the ethylenic linkage.

OXIDATION of acetylursolic acid with chromic acid has been investigated by Kuwada and Matsukawa (*J. Pharm. Soc. Japan*, 1933, **53**, 593), who obtained a product described as ketoacetylursolic acid, $C_{32}H_{48}O_5$, m. p. 296—297°; this substance gave an oxime, a semicarbazone, and a phenylhydrazone. Huzii and Osumi (*ibid.*, 1940, **60**, 291) repeated this oxidation and obtained a ketoacetylursolic acid, m. p. 347°, $[\alpha]_D$ +85°, which would not form an oxime. A consideration of the absorption spectrum of their product led them to the view that it is an αβ-unsaturated ketone.†

In our hands oxidation of acetylursolic acid with chromic anhydride gives ketoacetylursolic acid, $C_{32}H_{48}O_5$, m. p. 315—316°, $[\alpha]_D^{20°}$ +40·8°, which does not give a coloration with tetranitromethane in chloroform and exhibits an intense absorption maximum at 2500 A., $\varepsilon_{max.} = 13{,}000$, thus showing it to be an αβ-unsaturated ketone; the ketoacetyl acid is recovered unchanged after prolonged heating with alcoholic hydroxylamine. In these respects, ketoacetylursolic acid is similar to both α-amyrenonol and ketoacetyloleanolic acid. Oxidation of ethyl acetylursolate, m. p. 190—192°, with chromic anhydride gives *ethyl ketoacetylursolate*, m. p. 210—212°, which is identical with the ester prepared from ketoacetylursolic acid, m. p. 315—316°, by treatment with diazoethane. The ester, like the parent acid, does not give a coloration with tetranitromethane and exhibits the characteristic light absorption properties of an αβ-unsaturated ketone.

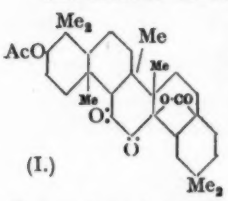
In addition to ketoacetylursolic acid, oxidation of acetylursolic acid gives a neutral fraction from which a *lactone*, $C_{32}H_{46}O_6$, has been isolated. Although it has only been possible to make a preliminary examination

* The fact that $)\overset{+}{C}H_2{\cdot}\bar{C}O_2$ is also a base in virtue of the carboxylate group is here irrelevant, and in any case the removal of this basicity by conversion of the carboxylate into the carboxyl group has little influence on the ease with which reaction takes place (Dawson and Pycock, *loc. cit.*).

† A comparison of the spectrographic properties of this compound and the ketoacetylursolic acid described by us has not been possible, since we have not had access to the original paper of the Japanese authors.

of this compound, we believe that its formation is of considerable significance in suggesting that the ethenoid linkage in ursolic acid is located in the near vicinity of the carboxyl group.* The lactone does not give a coloration with tetranitromethane, and exhibits an absorption maximum at 3100 A., $\varepsilon_{max.} = 7000$; when heated with N-alcoholic potassium hydroxide solution, it yields an alkali-soluble product; acidification of the alkaline solution (but not dilution of an aqueous alkaline solution with water) gives a neutral product; the amount of this hydrolysed neutral product was not sufficient for analysis.

The lactone bears a marked similarity to the isomeric " acetyldiketolactone " [(I) based on the Haworth variant of the hydropicene structure for oleanolic acid] obtained by oxidation of methyl ketoacetyloleanolate (Ruzicka, van der Sluys-Veer, and Cohen, *Helv. Chim. Acta*, 1939, **22**, 350); our lactone differs from that obtained from oleanolic acid in that, although the location of the absorption maximum is approximately the same in each case, the intensity of absorption of the lactone from ursolic acid is considerably greater than that from oleanolic acid.



(I.)

When heated with quinoline, ketoacetylursolic acid loses the elements of formic acid and gives *nor-α-amyradienonyl acetate*, $C_{31}H_{46}O_3$, m. p. 203—205°. Nor-α-amyradienonyl acetate gives a yellow coloration with tetranitromethane and exhibits an absorption maximum at 3000 A., $\varepsilon_{max.} = 10{,}000$, and in these and other respects shows a similarity to nor-β-amyradienonyl acetate (Ruzicka, Cohen, Furter, and van der Sluys-Veer, *Helv. Chim. Acta*, 1938, **21**, 1735). That the two substances are distinct was shown by the great depression in m. p. observed when the two compounds were mixed. Another case of similarity in physical constants of corresponding derivatives of α- and β-amyrin has been recorded by Ruzicka and Jeger (*Helv. Chim. Acta*, 1941, **24**, 1178), who find that β-amyrandionyl acetate prepared by oxidation of β-amyranonyl acetate with selenium dioxide has almost the same physical properties as the α-amyrandionyl acetate previously prepared by us (J., 1940, 1196) by the ozonolysis of α-amyradienyl acetate. Although a direct comparison of the two has not yet been possible, in our opinion it is unlikely that they will prove to be identical, since this would apparently require the identity of the distinct α-amyradienol and β-amyradienol-I.

Using the same reasoning as in the cases of β-amyradienonol (Picard and Spring, J., 1941, 35) and nor-β-amyradienonol (Ruzicka, Cohen, Furter, and van der Sluys-Veer, *loc. cit.*) it is clear that nor-α-amyradienonol contains the chromophoric system O:C·C:C·C:C and that *the carboxyl group of ursolic acid is in the vicinity of the ethenoid linkage.*

Experimental.

Ursolic acid, obtained from a crude apple pomace extract, was purified by Drake and Duval's method (*J. Amer. Chem. Soc.*, 1936, **58**, 1687) and after four crystallisations from alcohol separated in long fine needles, m. p. 283—284° (Found: C, 78·7; H, 10·5. Calc. for $C_{30}H_{48}O_3$: C, 78·9; H, 10·6%). Acetylursolic acid was obtained from alcohol in needles, m. p. 289—290°, $[\alpha]_D^{20°}$ +61·5° ($l = 1$, $c = 0{\cdot}9$ in chloroform) (Found: C, 77·3; H, 9·7. Calc. for $C_{32}H_{50}O_4$: C, 77·1; H, 10·0%).

Ethyl acetylursolate was obtained by treatment of acetylursolic acid (10 g.) with an ethereal solution of diazoethane prepared from nitrosoethylurea (12 g.). The ester separated from acetone in short prismatic needles, m. p. 190—192°, $[\alpha]_D^{20°}$ +63° ($l = 1$, $c = 3{\cdot}2$ in chloroform). Sell and Kremers (*J. Biol. Chem.*, 1937, **125**, 451) prepared ethyl acetylursolate by the action of ethyl alcohol on acetylursolyl chloride and record m. p. 194°, $[\alpha]_D$ +60·8°.

Ketoacetylursolic Acid.—A boiling solution of acetylursolic acid (8 g.) in glacial acetic acid (200 c.c.) was treated with a solution of chromic acid (6 g.) in acetic acid (50 c.c.; 85%) added during 5 minutes. The solution was refluxed for 90 minutes, diluted with water, and extracted with ether. After washing with water, the extract was washed with aqueous potassium hydroxide solution (20%), an insoluble potassium salt separating at the interface. The salt was collected, and the ethereal solution again washed with alkali and with water. Removal of the ether from the dried (sodium sulphate) solution gave a solid which after four crystallisations from chloroform–alcohol yielded the *lactone* in colourless silky needles, m. p. 305—306° (decomp.). *Light absorption in alcohol:* Maximum at 3120 A., $\varepsilon_{max.} = 7000$ (Found: C, 72·9, 72·9; H, 8·9, 8·7. $C_{32}H_{44}O_5$ requires C, 73·0; H, 8·8%).

The potassium salt was dissolved in hot alcohol (30 c.c.; 95%), and the solution filtered and acidified to Congo-red with hydrochloric acid. After dilution with water, the precipitated acid was collected, digested with boiling water, and, after drying, crystallised from chloroform–methanol. After two recrystallisations from the same solvent, *ketoacetylursolic acid* (3·2 g.) separated in colourless prisms, m. p. 315—316° (decomp.), $[\alpha]_D^{20°}$ +40·8° ($l = 0{\cdot}5$, $c = 0{\cdot}6$ in chloroform). It was very sparingly soluble in alcohol, but readily soluble in ether and chloroform. *Light absorption in alcohol:* Maximum at 2500 A., $\varepsilon_{max.} = 13{,}300$ (Found: C, 75·0; H, 9·2. $C_{32}H_{48}O_5$ requires C, 75·0; H, 9·4%).

Ethyl Ketoacetylursolate.—(*a*) This *ester* was prepared by the action of an ethereal solution of diazoethane on ketoacetylursolic acid; it separated from aqueous methanol in feather-like masses of fine needles, m. p. 210—212°, $[\alpha]_D^{20°}$ +92° ($l = 1$, $c = 1{\cdot}1$ in chloroform) (Found: C, 75·3; H, 9·75. $C_{34}H_{52}O_5$ requires C, 75·55; H, 9·6%).

(*b*) A solution of ethyl acetylursolate (11 g.) in boiling acetic acid (200 c.c.) was treated with a solution of chromic anhydride (8 g.) in acetic acid (50 c.c., 85%) added during 10 minutes. The mixture was refluxed for 2 hours, and the neutral product isolated in the usual manner. Ethyl ketoacetylursolate separated in fine needles from aqueous methanol and in prismatic needles from ethyl alcohol, m. p. 210—212°, undepressed in admixture with the specimen obtained as described in (*a*). *Light absorption in alcohol:* Maximum at 2500 A., $\varepsilon_{max.} = 12{,}000$.

Nor-α-amyradienonyl Acetate.—Ketoacetylursolic acid (1 g.) was refluxed with quinoline (40 c.c.) for 2 hours. The cooled solution was poured into excess of dilute hydrochloric acid, and the mixture extracted with ether. The extract was washed with dilute hydrochloric acid, and with sodium carbonate solution, a sodium salt then separating. The salt was collected and converted into the corresponding acid, which was identified as unchanged ketoacetylursolic acid by m. p. and mixed m. p. The residual ethereal solution was dried, and the neutral resin dissolved in alcohol, from which long flat yellow plates separated. After three recrystallisations (charcoal) from alcohol *nor-α-amyradienonyl acetate*

* Kuwada and Matsukawa (*loc. cit.*) have reported the formation of a neutral product—possibly a lactone—by the oxidation of ursolic acid with chromic anhydride and Huzii and Osumi (*loc. cit.*) claim that reduction of ketoursolic acid with sodium and alcohol yields a dehydrolactone, $C_{30}H_{46}O_3$.

separated in colourless plates, m. p. 203—205°, $[\alpha]_D^{21°}$ +41° (l = 0·5, c = 0·7 in chloroform). *Light absorption in alcohol :* Maximum at 3000 A., $\varepsilon_{max.}$ = 10,000 (Found : C, 79·3, 79·5; H, 10·1, 10·0. $C_{21}H_{44}O_3$ requires C, 79·8; H, 9·9%).

Grateful acknowledgment is made to the Carnegie Trust for a scholarship which enabled one of us (E. S. E.) to participate in this investigation. Our thanks are also due to Dr. K. S. Markley of the Bureau of Chemistry and Soils, U.S. Department of Agriculture, for the gift of an apple pomace extract.

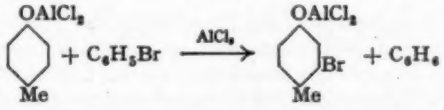
THE UNIVERSITY, MANCHESTER. [*Received, August 12th*, 1942.]

140. *The Action of Aluminium Chloride on Some Aromatic Bromo-compounds.*

By G. BADDELEY and J. PLANT.

Bromine atoms are shown to migrate to the nuclear positions of greatest electron density as indicated by nuclear alkylation.

BROMOBENZENE is a brominating agent in the presence of aluminium chloride, some *p*-dibromobenzene being formed; with *p*-tolyloxyaluminium chloride (from *p*-cresol), it affords benzene and 2-bromo-*p*-cresol :



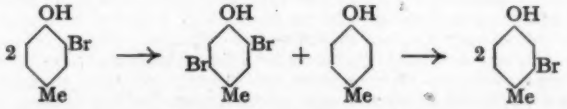
The combined reagents acting upon phenol produce considerable alkali-insoluble products but no bromophenol.

The three bromophenols give *p*-bromophenol (*ca.* 70%), phenol (*ca.* 17%), and higher-boiling products; the isomerisation of *o*-bromophenol is readier than that of the *m*-isomer. *p*-Bromophenol with *p*-cresol (1 mol.) and excess of aluminium chloride produce a mixture of approximately equal amounts of both reactants, phenol, and 2-bromo-*p*-cresol.

The products of the action of aluminium chloride (2 mols.) on 3-bromo-*p*-cresol are shown in the following table :

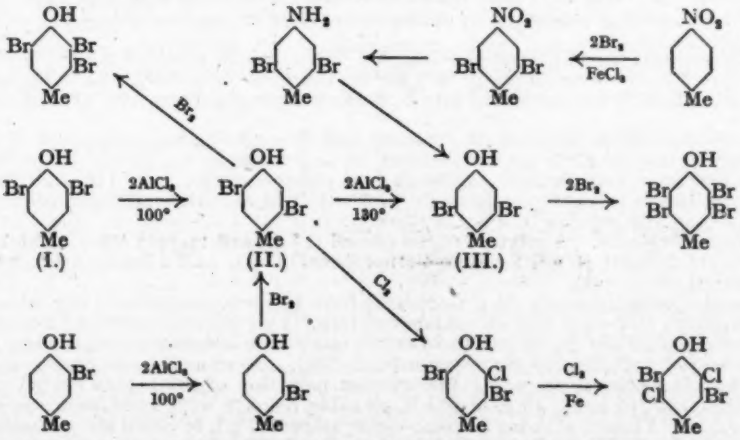
		Products, %.			
Temp.	Time (hrs.).	3-Bromo-*p*-cresol.	2-Bromo-*p*-cresol.	2 : 6-Dibromo-*p*-cresol.	*p*-Cresol.
100°	20	33	60	3	3
127	1	—	67	6	8
115	0·75	—	45	—	—

The 2-bromo-*p*-cresol is formed, no doubt, in the following steps :



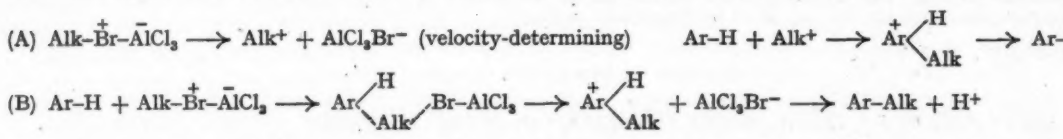
The more rapid isomerisation of 2-bromo- to 3-bromo-4-ethylphenol is probably due to the induced nucleophilic condition of the 3-position of 4-ethylphenol being greater than that of the corresponding 2-position of *p*-cresol.

At 100° 3 : 5-dibromo-*p*-cresol (I) isomerises to the 2 : 5-*dibromo*-derivative (II), and at 130° this in turn is converted into the 2 : 6-*dibromo*-compound (III). The products are identified as shown in the following scheme :



2 : 6-Dibromo-4-ethylphenol isomerises to the 3 : 5-*dibromo*-compound at 120°.

These brominations by aromatic bromo-compounds are in marked contrast with the alkylations by alkyl bromides in the presence of aluminium chloride. Whether the latter reactions involve a uni- or a bi-molecular mechanism, (A) or (B) respectively, the complex $Ar–\overset{+}{B}r–\overset{-}{A}lCl_3$ is unlikely to behave in a similar manner since



(i) nuclear-attached halogen is firmly held and, in consequence, the unimolecular reaction is unlikely; and (ii) the induced electrophilic properties of the aromatic nucleus are distributed and so offer little encouragement for the bimolecular reaction. Apparently the electrophilic properties of the bromine atoms exceed those induced at any one position in the nucleus. The bromine atoms tend to move to the positions of greatest electron density and show little tendency to pile up in a few nuclei (as is the case with alkylation), since bromine atoms (especially in the presence of aluminium chloride) lower the electron density of the aromatic nuclei to which they are attached.

The positions taken up by the bromine atoms are those which are preferentially alkylated. For instance, alkylation of phenol occurs first in the *p*-position, and *o*- and *m*-bromophenols produce the *p*-isomeride; further, alkylation and bromination of a phenol homologue are both directed by the alkyl group and not the oxygen atom. This difference from the acylation of a phenol nucleus is readily explained by the difference in the vigour of the electrophilic attack, only the acylation being capable of developing the electromeric effect of the phenolic oxygen atom to a degree at which it can supersede the directing power of alkyl groups.

2-Chlorophenol and 3 : 5-dichloro-*p*-cresol are not isomerised by aluminium chloride. Chloro-2-bromophenol produces the 3-bromo-derivative, thus indicating that the directing power of the chlorine atom can compete successfully with that of the oxygen atom.

Experimental.

Reactions with Aluminium Chloride.—Bromobenzene. Pure bromobenzene (26 g.) and the chloride (25 g., 1 mol.) were heated together at 100° for 1·5 hours. Decomposition with ice produced bromobenzene (13 g.) and *p*-dibromobenzene (2 g.; m. p. and mixed m. p. 89°).

Bromobenzene and p-*cresol.* A mixture of *p*-cresol (22 g., 1 mol.), bromobenzene (31 g., 1 mol.), and the chloride (80 g., 2 mols.) was heated at 100° for 2 hours. After decomposition with ice and separation of a red precipitate, there were obtained (i) an alkali-insoluble fraction containing benzene (1 g.), bromobenzene (1 g.), and higher-boiling products (30 g.), and (ii) an alkali-soluble fraction containing *p*-cresol (11·5 g.) and 2-bromo-*p*-cresol (2 g.).

A mixture of phenol (16 g.), bromobenzene (26 g.), and reagent (70 g.), treated as above, afforded (i) an alkali-insoluble fraction, of which only 2 g. were distillable (b. p. 160—180°/25 mm.), and (ii) 6 g. of phenol.

2-Bromophenol. A mixture of the phenol (15 g.) and reagent (25 g., 2 mols.) was heated at 130° for 1 hour. Phenol (1·5 g.), 4-bromophenol (10·5 g.; benzoate, m. p. and mixed m. p. 102°), and a higher-boiling fraction (1 g.) were obtained.

3-Bromophenol. Under precisely the same conditions as for 2-bromophenol, this afforded phenol (1 g.), bromophenol (10 g.; crystallisation of the benzoate from alcohol gave first plates and then needles which were identified as the benzoates of 4-bromo- and of 3-bromophenol respectively), and a higher-boiling fraction (2 g.).

4-Bromophenol. Under the above conditions, phenol (1 g.), 4-bromophenol (10·5 g.), and a higher-boiling fraction (2 g.) were obtained.

4-Bromophenol and p-*cresol.* A mixture of 4-bromophenol (34·5 g., 1 mol.), *p*-cresol (21·6 g., 1 mol.), and aluminium chloride (112 g., 4 mols.) was heated at 130° for 3·5 hours and subsequently decomposed with ice. Phenol (12 g.), *p*-cresol (11 g.), 4-bromophenol (11 g.), 2-bromo-*p*-cresol (15 g.), and higher-boiling fractions (4 g.) were obtained.

*3-Bromo-*p-*cresol.* (i) A mixture of the cresol (45 g.) and reagent (65 g., 2 mols.) was heated at 127° for 1 hour. *p*-Cresol (2 g.), 2-bromo-*p*-cresol (31 g.; m. p. and mixed m. p. 55°), and 2 : 6-dibromo-*p*-cresol (4 g.; m. p. and mixed m. p. 109°) were obtained. (ii) From 143 g. and 190 g. respectively of the same substances, heated at 100° for 17 hours, there were obtained 2, 86, and 7 g., respectively, of the same products, together with 47 g. of unchanged 3-bromo-*p*-cresol.

*Preparation of 2-Bromo- and 2 : 6-Dibromo-*p-*cresol.*—Dr. Short kindly provided a sample of 2-bromo-*p*-toluidine, which was converted into 2-bromo-*p*-cresol (m. p. 55°) and its benzoate (m. p. 76°). 2 : 6-Dibromo-*p*-toluidine (Nevile and Winther, *Ber.*, 1880, **13**, 973) was converted into 2 : 6-*dibromo*-p-*cresol*, m. p. 109° (Found : Br, 59·9. $C_7H_6OBr_2$ requires Br, 60·1%).

2-Bromo-4-ethylphenol.—Bromine (32 g.) in glacial acetic acid (10 c.c.) was gradually added (2 hours) to a vigorously stirred solution of 4-ethylphenol (25 g.) in the same solvent (50 c.c.) cooled by tap water. The mixture was then heated on the steam-bath for 0·25 hour, and distilled. 2-Bromo-4-ethylphenol (33 g.; b. p. 116—120°/20 mm.) was obtained; its p-*nitrobenzoate* crystallised from light petroleum (b. p. 60—80°) in colourless radiating needles, m. p. 57° (Found : N, 4·2; Br, 22·3. $C_{15}H_{13}O_4NBr$ requires N, 4·0; Br, 22·8%).

Reaction with aluminium chloride. A mixture of the phenol (17 g.) and reagent (26 g., 2 mols.), heated at 100° for 1·25 hours, afforded 4-ethylphenol (1 g.), 2-bromo-4-ethylphenol (5 g.), and 3-bromo-4-ethylphenol (9 g.; *p*-nitrobenzoate, m. p. and mixed m. p. 108°).

3-Bromo-4-ethylphenol.—3-Bromoanisole (51 g.; prepared from 3-bromonitrobenzene) was mixed with acetyl chloride (23 c.c.) in carbon disulphide (150 c.c.), and aluminium chloride (75 g.) gradually added. 3-Bromoanisole (15 g.) and 2-bromo-4-methoxyacetophenone (39 g.; b. p. 148—156°/15 mm.) were obtained. This ketone gave a *semicarbazone*, m. p. 198° (Found : N, 14·8. $C_{10}H_{12}O_2N_2Br$ requires N, 14·7%), and some 3-bromophenol on demethylation with hydrobromic acid (*d* 1·5) in glacial acetic acid. Clemmensen reduction of the ketone (38 g.) gave 3-bromo-4-ethylanisole (24 g.; b. p. 123—124°/15 mm.), 10 g. of which, on being refluxed with hydrobromic acid (*d* 1·5; 22 c.c.) and glacial acetic acid (70 c.c.) for 3 hours, afforded 3-bromo-4-ethylphenol (7 g.), of which the p-*nitrobenzoate* had m. p. 108° (Found : N, 4·2; Br, 22·65. $C_{15}H_{13}O_4NBr$ requires N, 4·0; Br, 22·8%) after recrystallisation from light petroleum (b. p. 60—80°).

3 : 5-*Dibromo*-p-*cresol and Aluminium Chloride.*—(i) A mixture of the phenol (12 g.) and reagent (12 g., 2 mols.), when heated at 130° for 1 hour, gave 2 : 6-dibromo-*p*-cresol (10 g.), which recrystallised from light petroleum (b. p. 60—80°) in long, fine needles, m. p. and mixed m. p. 109°; on treatment with excess of bromine in acetic acid, this afforded 2 : 3 : 5 : 6-tetrabromo-*p*-cresol, m. p. and mixed m. p. 199°. (ii) When 50 and 55 g., respectively, of the reagents were heated at 100° for 24 hours, they yielded 2 : 5-*dibromo*-p-*cresol* (28 g.), which crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 61° (Found: Br, 60·2. $C_7H_6OBr_2$ requires Br, 60·1%), 2 : 6-dibromo-*p*-cresol (12 g.), and a residue (10 g.). The former cresol and excess of bromine in acetic acid gave 2 : 3 : 5-tribromo-*p*-cresol, m. p. 101° (Found: Br, 69·5. Calc. for $C_7H_5OBr_3$: Br, 69·5%) (Zincke and Wiederhold, *Annalen*, 1901, **320**, 205, give m. p. 102°).

Bromine (46 g.) was gradually added (0·75 hour) to a solution of 3-bromo-*p*-cresol (54 g.) in glacial acetic acid (70 c.c.). Fractional distillation gave 2 : 5-dibromo- (61 g.; m. p. 61°) and 2 : 3 : 5-tribromo-*p*-cresol (10 g.; m. p. 101°). Chlorine was bubbled through a solution of the former (20 g.) in carbon tetrachloride (10 c.c.) for 2 hours and 3-*chloro*-2 : 5-*dibromo*-p-*cresol* (25 g.; m. p. 95° after recrystallisation from alcohol) (Found: Cl, 11·8; Br, 53·8. $C_7H_5OClBr_2$ requires Cl, 11·8; Br, 53·3%) was obtained. This substance (10 g.) was dissolved in carbon tetrachloride (30 c.c.), and iron powder (2 g.) added. Chlorine was bubbled through the mixture at 70—80° for 40 mins., and 3 : 6-dichloro-2 : 5-dibromo-*p*-cresol (11 g.) was obtained, m. p. 177—178° (Zincke and Buff, *Annalen*, 1905, **341**, 340, give m. p. 175—176°). This substance on analysis (Viebock, *Ber.*, 1932, **65**, 586) produced halogen acids equivalent to 6·10 c.c. of N/40-sulphuric acid (Calc. for $C_7H_4OCl_2Br_2$: 6·07 c.c.).

A mixture of 3 : 6-dibromo-*p*-cresol (15 g.) and aluminium chloride (20 g.) produced the 2 : 6-dibromo-derivative (14 g.) after 1 hour at 130°.

2 : 6-*Dibromo*-4-*ethylphenol.* Bromine (3·75 c.c.) in glacial acetic acid (5 c.c.) was gradually added to a cooled solution of 2-bromo-4-ethylphenol (14·5 g.) in glacial acetic acid (20 c.c.) and gave 2 : 6-dibromo-4-ethylphenol (14 g.); its p-*nitrobenzoate* crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 93° (Found: N, 3·4; Br, 37·0. $C_{15}H_{11}O_4NBr_2$ requires N, 3·3; Br, 37·3%).

Reaction with aluminium chloride. A mixture of this phenol (5 g.) and the reagent (5 g.), when heated at 120° for 1·5 hours, gave the unchanged phenol (2 g.) and 3 : 5-*dibromo*-4-*ethylphenol* (2 g.), which crystallised from light petroleum (b. p. 60—80°) in clusters of radiating needles, m. p. 116—117° (Found: Br, 57·1. $C_8H_8OBr_2$ requires Br, 57·1%). Excess of bromine in glacial acetic acid gave 2 : 3 : 5 : 6-tetrabromo-4-ethylphenol, m. p. 106° (Fittig and Kiesow, *Annalen*, 1870, **156**, 255, give m. p. 105—106°).

Chloro-2-bromophenol and Aluminium Chloride.—A mixture of the phenol (14 g.) and the chloride (21 g., 2 mols.) was heated at 125° for 2·5 hours, affording unchanged phenol (4 g.) and 4-chloro-3-bromophenol (4 g.), which crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 65°. This substance was also prepared from 4-chloro-3-bromoaniline.

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141. *The Action of Aluminium Chloride on Some Phenol Homologues.*

By G. BADDELEY.

The interconversions of *p*- and *m*-cresols have been studied quantitatively, and a probable mechanism suggested. All the xylenols have been found to give ultimately *m*-5-xylenol, and this is explained. Hemimellithenol isomerises quantitatively to *iso*-ψ-cumenol. The three ethylphenols undergo internuclear alkyl-group migration with the formation of some phenol and 3 : 5-diethylphenol.

The interconversion of *p*- and *m*-xylenes is related to that of *p*- and *m*-cresols. The respective significances of intra- and inter-molecular migration in the action of aluminium chloride on the homologues of phenol and benzene are related and accounted for. Intermolecular migration is shown to be associated with a high nuclear electron availability, and *p*-cresol has been demethylated by toluene in the presence of aluminium chloride. A mechanism is deduced for the Scholl reaction.

MOLECULAR proportions of phenol and aluminium chloride furnish phenoxyaluminium chloride, which can be distilled under atmospheric pressure. *p*-Cresol yields a similarly stable derivative which remains unchanged after several hours at 200°. In the presence of more than one molecular proportion of aluminium chloride, however, even at 125°, partial conversion of *p*- into *m*-cresol occurs.

Kinetic study of this change showed it to be reversible and unimolecular in respect of *p*-tolyloxyaluminium chloride, but bimolecular in respect of the further aluminium chloride employed; the reagent is not used up in the course of the reaction, and the unimolecular velocity constant, at a given temperature, is proportional to the square of the amount of reagent present.

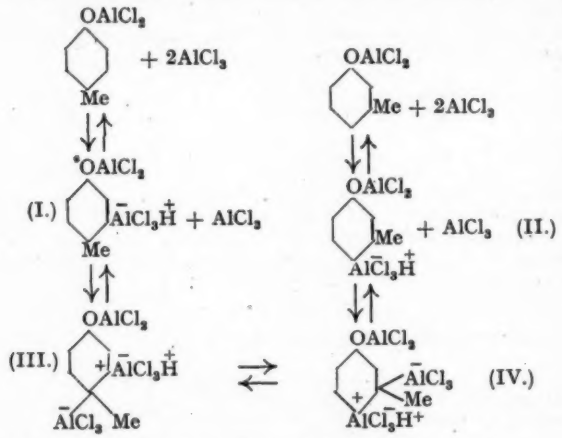
Unimolecular velocity constants for the interconversions p- $\underset{k_2}{\overset{k_1}{\rightleftharpoons}}$ m-*cresol at* 135° *with various amounts of aluminium chloride.*

$AlCl_3$, mols.	1·00	1·20	1·26	1·40	1·53	1·60
Excess $AlCl_3$	0	0·20	0·26	0·40	0·53	0·60
$k_1 + k_2$	0	0·053	0·094	0·25	0·42	0·51
1·44 (Excess $AlCl_3$)^2	0	0·058	0·097	0·23	0·41	0·52

The composition of the equilibrium mixture both at 125° and at 135° was approximately in the ratio 61 *m* : 39 *p*, so the heat of isomerisation is small. The range of temperature suitable for kinetic measurements is limited by the supervention of intermolecular reaction (see below), but from these results an activation energy of 22·5 kg.-cals. may be derived. In explanation of these results, the annexed scheme is proposed.

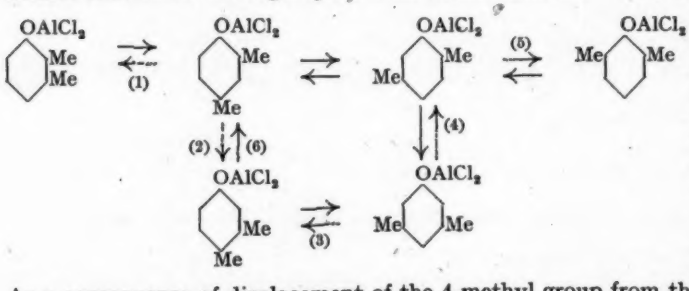
The oxyaluminochloride group has a strongly negative inductive effect, so the methyl group determines the site of attack of the tolyloxyaluminium chloride by electrophilic reagents, as in (I) and (II). Experimental confirmation of this deduction will be supplied later from the results of the alkylation and bromination

of *p*- and *m*-cresols in the presence of excess of aluminium chloride. Atomic models, however, show that steric conditions in (I) and (II) determine a displacement of either the methyl or the aluminium chloride group from the plane of the nucleus (cf. Baddeley, *Nature*, 1939, **144**, 444; 1942, **150**, 178), giving rise to polarisations which permit attachment of a further molecule of aluminium chloride to the carbon atom carrying the methyl group (Hampson and Ingham, J., 1939, 981). The interconversion of the resulting products (III) and (IV) is of the Wagner–Meerwein type.

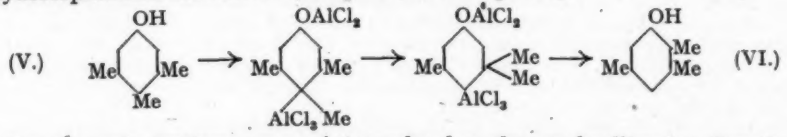


The strongly negative inductive effect of the oxyaluminochloride group is especially effective in the *o*-position, so that *o*-cresol is not isomerised under the conditions already discussed. Intranuclear migration of a methyl group in the *o*-position does, however, occur with the xylenols, and *m*-2-xylenol yields the *m*-5-isomeride. The lower mobility of the methyl group in the *o*-position, however, is illustrated by the conversion of *m*-4-xylenol into the *p*- and the *o*-3-isomeride, and of the latter into the *p*-isomeride.

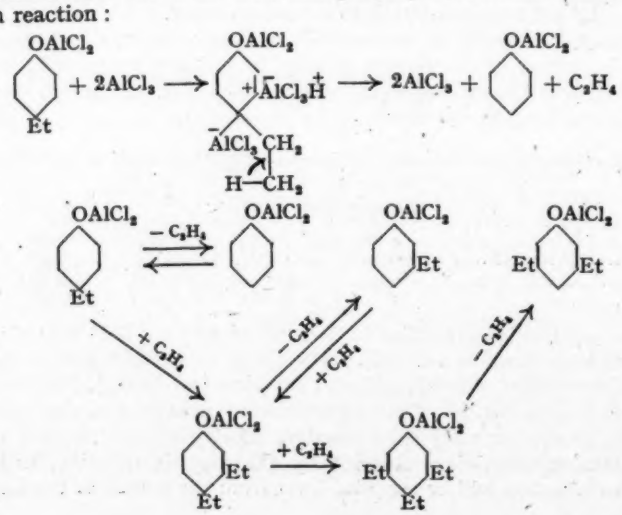
The behaviour of the xylenols towards aluminium chloride, whereby they all yield the *m*-5-isomeride, further illustrates the cogency of these considerations. Thus transformations (1), (2), and (3) are hindered, as indicated by the discontinuous arrows, by difficulty of the requisite attachment of aluminium chloride, whilst (4), (5), and (6) would require such attachment in an *o*-position to the oxyaluminochloride group. The changes which actually occur can be achieved at lower temperatures than in the cases of the cresols. Similarly, hemimellithenol (V) is converted even more readily at 100° into *iso*-ψ-cumenol (VI), and the application of the above considerations is again exemplified.



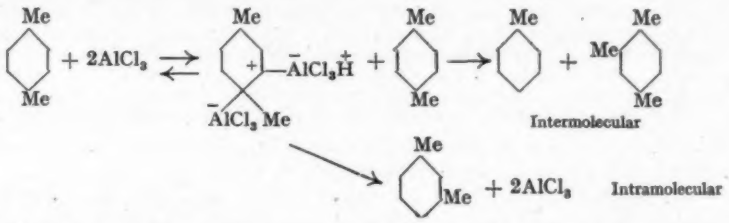
As a consequence of displacement of the 4-methyl group from the plane of the nucleus by those in the 3- and the 5-position, attachment of aluminium chloride causes a migration of the alkyl group comparable with that observed with oxyacetophenone derivatives (compare this vol., p. 273).



At 170° the three cresols undergo some intermolecular change leading to phenol and *m*-5-xylenol: $2C_6H_4Me\cdot OH \rightarrow C_6H_5\cdot OH + C_6H_3Me_2\cdot OH$. This type of reaction predominates when the three ethylphenols are treated with aluminium chloride even at 100°, and possibly involves intermediate formation of ethylene by a species of Hofmann reaction:



The familiar simultaneous intra- and inter-molecular changes of benzene homologues may be interpreted in the same manner as those of the phenols :



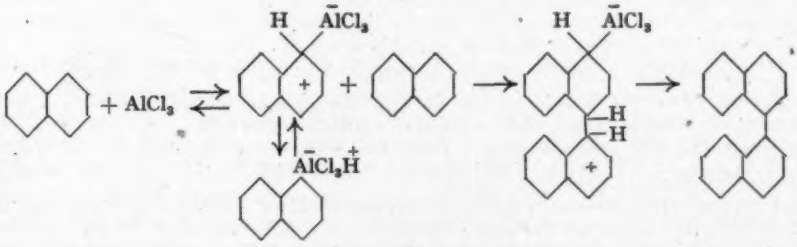
The following table shows the relative significance of intra- and inter-molecular migrations of alkyl groups in the isomerisations of some homologues of phenol and benzene :

Phenols.	Convenient temperatures for : Intramolecular migration.	Intermolecular migration.
2-Me	None	170°
3-Me; 4-Me	135°	170
Xylenols	120	150
3 : 4 : 5-Me_3	100	?
2-Et; 3-Et; 4-Et	?	100
Benzene		
All homologues	100	100

The readiness of the intermolecular increases more readily on descending the table than does that of the intramolecular migrations; only above the broken line can the separate occurrence of intramolecular isomerisations be procured.

The sequence benzene homologues, xylenols, cresols, phenol is one of decreasing electron availability (nucleophilic character) in the presence of excess of aluminium chloride. The obvious connection between a high electron availability of the nucleus and a ready intermolecular migration suggests that a molecule in a suitable condition to undergo a Wagner–Meerwein rearrangement can also suffer a Hofmann degradation in the presence of an aromatic nucleus of sufficient electron availability. Phenol homologues should thus isomerise less readily in the presence of a benzene homologue, since this is preferentially attacked by the aluminium chloride. Further, if the reagent is still able to attack the phenol nucleus and so produce a mobile methyl group, this should undergo nucleophilic attack by the benzene homologue. This possibility has been realised : *p*-cresol is partly demethylated when heated at 135° with toluene and an excess of aluminium chloride, although in the absence of toluene it suffers no demethylation at this temperature. The xylene primarily formed is, of course, converted into a mixture of hydrocarbons as usual. It should be further noted that under these conditions no detectable quantity of *m*-cresol is formed.

These researches originated from a suggestion that the Scholl dehydrogenation reaction was direct radical formation (Kenner, *J. Soc. Chem. Ind.*, 1933, **42**, 470). Later, the possibility of its being an ordinary case of substitution was pointed out (Baddeley and Kenner, J., 1935, 307), and this is in accord with the above considerations :



Experimental.

Phenol and Aluminium Chloride.—After phenol (19 g.) and aluminium chloride (29 g., 1 mol.) had been warmed together until hydrogen chloride evolution ceased, the residue melted at 175—180° and distilled at 210°/15 mm. (Found : Cl, 37·0. Calc. for $C_6H_5{\cdot}OAlCl_2$: Cl, 37·2%). After crystallisation from carbon disulphide it melted at 183° and was thus identical with the product of the same composition prepared by Perrier (*Bull. Soc. chim.*, 1896, **15**, 1181). It suffered slight decomposition when distilled at 310°/760 mm., yielded phenol on treatment with water, and hydrogen chloride when treated with a second and a third molecular proportion of phenol.

Isomerisation of p-*Cresol.*—A mixture of *p*-cresol (32 g.) and aluminium chloride (84 g.) was gradually heated to 130°. It first melted and then set to a solid mass, with liberation of hydrogen chloride. After 0·5 hour at 130°, the mixture had become a homogeneous, pale yellow oil which slowly darkened on prolonged heating. After 2 hours, the molten mixture was cooled to 60° and poured on ice. The product was distilled with steam, the distillate extracted with ether, the extract dried over calcium chloride, the ether removed, and the residue distilled; b. p. 106°/15 mm.

(25 g.). The product did not solidify when seeded with *p*-cresol at − 10°. The benzoate, recrystallised from ethyl alcohol, was identified as that of *m*-cresol (benzoate, m. p. and mixed m. p. 54°).

As a preliminary to a kinetic study of the change, the quantitative analysis of mixtures of the two cresols by the bromination method was examined, and the following procedure adopted: 5 c.c. of a solution of the mixture in 50% aqueous acetic acid (15 g./l.) was diluted with a further 15 c.c. of the 50% acid. Carbon tetrachloride (1 c.c.), N-potassium bromate–bromide solution (5 c.c.), and 5N-hydrochloric acid (5 c.c.) were then successively added, and the mixture well shaken for 1 minute. After addition of potassium iodide (0·5 g.), free iodine was titrated with 0·2N-thiosulphate solution. The following is typical of the experiments carried out on this basis; k is calculated from $k = (1/t) \log_e (T_0 - T_\infty)/(T_t - T_\infty)$, where t is the time in hours and T is the titre, the subscripts having the conventional significance.

p-Cresol (36 g.) and aluminium chloride (56 g.; 1·25 mols.) were shaken together at approx. 130° for 40 mins., and the clear solution then placed in a thermostat at 135°.

t, hrs.	Wt. of sample, g.	50% HOAc, c.c.	*T*, c.c.	10^3k.	*t*, hrs.	Wt. of sample, g.	50% HOAc, c.c.	*T*, c.c.	10^3k.
0	1·812	45·6	8·20	—	10·6	1·760	44·0	5·56	93
0·5	1·789	44·7	8·02	87	14·2	1·771	44·3	5·07	96
1·5	1·751	43·8	7·65	93	19·4	1·854	46·4	4·67	95
2·0	1·966	49·2	7·47	95	34·0	2·520	63·0	4·15	98
5·5	1·879	47·0	6·50	94	∞	—	—	4·00	—
8·0	1·889	47·2	5·97	95					Mean 94

Equilibrium mixture. (i) The mixture of cresols was recovered after 34 hours at 135°, and 4·500 g. were made up to 250 c.c. with 50% aqueous acetic acid; 5 c.c. of this solution required 4·34 c.c. of bromate–bromide solution, whereas a similar solution made from pure *m*-cresol required 5·03 c.c. The mixture contained 58·9% of *m*- and 41·1% of *p*-cresol. Therefore the composition of the equilibrium mixture is 60·7% of *m*- and 39·3% of *p*-cresol.

(ii) *p*-Cresol (36 g.) was shaken with aluminium chloride (90 g.) at 135° for 15 mins., and the clear solution decanted from undissolved aluminium chloride. The velocity constant at 135° was 0·76 and the equilibrium mixture contained 60·8% of *m*- and 39·2% of *p*-cresol, so the composition is independent of the proportion of aluminium chloride.

(iii) A mixture of *m*-cresol (36 g.) and aluminium chloride (68 g.) gave $k_{135°} = 0·42$ and an equilibrium mixture of 61·0% of *m*- and 39·0% of *p*-cresol, *i.e.*, the same as above.

Energy of Activation of the Isomerisation.—A homogeneous mixture of *p*-cresol (72 g.) and aluminium chloride (136 g.) was divided between two flasks, and the velocity constants determined at 125° and at 135°: $k_{125°} = 0·21$; $k_{135°} = 0·42$; hence $E = 22·5$ kg.-cals. The values of T_∞ for the two experiments were identical.

Mixtures of *p*-cresol (8·09 g.) and 12·0, 14·0, and 16·0 g. of aluminium chloride gave respectively $k_{135°} = 0·053, 0·251$, and 0·506.

o-*Cresol and Excess of Aluminium Chloride.*—(*a*) *o*-Cresol (32 g.) and aluminium chloride (84 g., 2 mols.) were heated together at 130° for 3 hours, but pure *o*-cresol was recovered almost quantitatively. (*b*) *o*-Cresol (11 g.) and aluminium chloride (30 g.) were heated together at 170° for 5 hours, and the product poured on ice and distilled with steam. There was considerable non-volatile material. The distillate was extracted with ether, and the extract dried over calcium chloride and distilled: (i) b. p. 180—200° (1·5 g.), identified as phenol by its *p*-nitrobenzoate; (ii) b. p. 200—210° (2·5 g.), contained some phenol; (iii) b. p. 210—215° (1·5 g.), identified as *m*-5-xylenol by its *p*-nitrobenzoate.

Both *m*- and *p*-cresol gave small amounts of phenol, etc., under these conditions.

Reactions of Xylenols with Aluminium Chloride.—m-2-*Xylenol.* This xylenol (12 g.) and aluminium chloride (30 g., 2 mols.) were heated together at 130—135° for 4·5 hours, and the product worked up in the usual manner; b. p. 212° (10 g.). The solid (*m*-5-xylenol) recrystallised from petroleum (b. p. 60—80°) in stout needles, m. p. 64°; *p*-nitrobenzoate, m. p. and mixed m. p. 109°.

m-4-*Xylenol.* This xylenol (25 g.) and aluminium chloride (60 g., 2 mols.) were heated together at 115—120° for 2 hours. After the usual procedure, the product was fractionally distilled under 15 mm.: (i) B. p. 106° (15 g.), identified as original xylenol by *p*-nitrobenzoate. (ii) B. p. 110° (6 g.); preparation of the *p*-nitrobenzoate showed this fraction to contain both *m*-4- and *p*-xylenol. [The *p*-nitrobenzoate of the latter is more soluble in petroleum (b. p. 60—80°) than is that of the former.] (iii) B. p. 112—115° (3 g.); the *p*-nitrobenzoate after three crystallisations gave the pure derivative of *o*-3-xylenol, m. p. and mixed m. p. 104·5°.

m-4-Xylenol (20 g.) and aluminium chloride (50 g.) were heated together at 130—135° for 4·5 hours. After the usual procedure, the final product was distilled; b. p. 212° (16 g.). The semi-solid was recrystallised from petroleum (b. p. 60—80°) and identified as *m*-5-xylenol (m. p. and mixed m. p. 64°).

p-*Xylenol.* Under the conditions of the above experiment, *p*-xylenol (12 g.) and aluminium chloride (30 g.) gave a product, b. p. 212° (10 g.), identified as *m*-5-xylenol.

o-4-*Xylenol.* Under the above conditions, the xylenol (12 g.) and aluminium chloride (30 g.) produced fairly pure *m*-5-xylenol.

o-3-*Xylenol.* This xylenol (19 g.) and aluminium chloride (44 g.) were heated together at 120—125° for 4 hours. The final product obtained by the usual procedure was fractionated under 20 mm.: (i) B. p. 106—112° (10 g.), recrystallised from petroleum (b. p. 60—80°), was identified as *p*-xylenol, m. p. and mixed m. p. 74° (confirmed by means of the *p*-nitrobenzoate). (ii) B. p. 112—122° (4 g.), recrystallised from petroleum (b. p. 60—80°) and identified as *m*-5-xylenol. (iii) B. p. 130—300° (5 g.), a coloured oil not identified.

Reactions of Other Phenols with Aluminium Chloride.—*Hemimellithenol.* This phenol (1 g.) and aluminium chloride (3 g.) were heated together at 100° for 10 hours and then poured on ice. The solid obtained, m. p. 95° after recrystallisation, did not depress the m. p. of *iso*-ψ-cumenol, m. p. 95°.

4-*Ethylphenol.* This phenol (18 g.) and aluminium chloride (50 g.) were heated together at 120° for 4 hours. The final product, obtained in the usual way, was fractionally distilled: (i) b. p. 190—208° (4 g.), almost pure phenol; (ii) b. p. 208—218° (4 g.), a mixture containing some phenol; (iii) b. p. 218—228° (4 g.), did not give a solid *p*-nitrobenzoate and was not identified; (iv) b. p. 228—238° (4 g.) and (v) b. p. 238—240° (2 g.) were recrystallised from petroleum (b. p. 60—80°) and identified as 3 : 5-diethylphenol, m. p. and mixed m. p. 77°.

3-*Ethylphenol.* This phenol (4 g.) and aluminium chloride (10 g.) were heated together at 125° for 2 hours; the subsequent procedure was as usual: (i) b. p. 85°/20 mm. (1 g.), phenol; (ii) b. p. 110—115°/20 mm. (1·5 g.), did not give a solid *p*-nitrobenzoate and was not identified; (iii) b. p. 130—135°/20 mm. (1 g.), identified as 3 : 5-diethylphenol.

2-, 3-, and 4-*Ethylphenols at* 100°. Under conditions as for 4-ethylphenol, but at 100°, the products were the same as those from that phenol.

3-*Methyl*-4-*ethylphenol.* This phenol (5 g.) and aluminium chloride (10 g.) were heated together at 100° for 18 hours, and poured on ice, affording 3-methyl-5-ethylphenol.

Interaction of p-*Cresol and Toluene in the Presence of Aluminium Chloride.*—A mixture of *p*-cresol (43 g.), toluene (37 g.),

and aluminium chloride (108 g.) was heated at 135° for 5 hours. Considerable decomposition occurred. The product was poured on ice, and extracted with ether. The extract was washed with sodium hydroxide, and the alkali-soluble product consisted of approximately equal parts of phenol and *p*-cresol (10 g. of each were obtained by fractional distillation and identified by their m. p. and mixed m. p. and also by the m. p. and mixed m. p. of their *p*-nitrobenzoates).

The author is indebted to Professor J. Kenner, F.R.S., for his interest in the work described in this and the preceding paper.

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142. *Rare-earth Metal Amalgams. Part IV. The Isolation of Europium.*

By JOSEPH K. MARSH.

Europium is concentrated rapidly by shaking its acetate (<1% Eu) with sodium amalgam, thus forming a samarium–europium amalgam and leaving gadolinium, etc., in solution (Part II; J., 1942, 398). The action of acetic and sulphuric acid on the amalgam is to give a pure samarium acetate solution and a samarous–europous sulphate precipitate. Nitric acid then selectively oxidises samarium, leaving europous sulphate (90%). This, when converted into acetate and then into amalgam and treated with concentrated hydrochloric acid, yields pure $EuCl_2,2H_2O$ crystals. If pure samarium is not desired, the acetate (<1% Eu) is shaken with a little sodium amalgam and sulphuric acid, and europous sulphate (20%) results. The solubility of this sulphate is less in acetate than in chloride solutions, and the stability of samarous sulphate is greater. An advantage is thereby gained over McCoy's technique for europium purification. Applications of zinc, barium, and samarium amalgams to europium purification are also described.

YNTEMA (*J. Amer. Chem. Soc.*, 1930, **52**, 2782), using electroreduction, first showed that europium could be purified by precipitation of the bivalent sulphate. McCoy effected reduction by means of amalgamated zinc, but neither method was suited to quantitative separation from low concentrations. McCoy later reduced chloride solutions with zinc dust, and by co-precipitation with the less soluble but isomorphous barium sulphate obtained a large supply of purified europium material from a source, mainly samarium and gadolinium, but containing 0·5% of europium. His first concentrate does not appear to have contained more than 10% of europous sulphate, the rest being barium sulphate and much other rare-earth sulphates. Repeated reduction of chloride solutions with amalgamated zinc, followed by precipitation of bivalent sulphate, failed to remove the last few parts per 1000 of other rare earths, but later it was shown that europium of at least 70% content on reduction of a concentrated trichloride solution with amalgamated zinc yielded the dichloride, which was precipitated in a pure state on addition of concentrated hydrochloric acid (*ibid.*, 1935, **57**, 1756; 1936, **58**, 2279; 1937, **59**, 1131).

The method of concentrating europium now recommended makes use of acetate solutions. Europous sulphate is much less soluble in these than in chloride solutions. Moreover, samarous sulphate, being also less soluble and less ionised, is more stable in them and can be used as a co-precipitant of the europium in place of the hitherto-used barium sulphate, from which the recovery of europium is troublesome. A third advantage lies in the avoidance of the use of zinc dust, for finely divided metals render bivalent sulphate precipitates unstable.

From a crude rare-earth mixture, samarium and europium are removed together as amalgam by treatment with sodium amalgam (Part II, *loc. cit.*). If the original earths were largely samarium, europium, and gadolinium, gadolinium of good purity will constitute the non-amalgam-forming residue in the treated acetate solution. The samarium–europium amalgam is decomposed by mixed acetic and sulphuric acids to give mainly pure samarium(III) acetate and impure (20%) europium(II) sulphate. If, however, the isolation of europium alone is desired, the crude rare-earth solution is treated with small amounts of sulphuric acid and sodium amalgam. In presence of a strong acid, samarium–europium amalgam formation is small, and in the above reaction a precipitate of mixed europous and samarous sulphates results, similar to that yielded by treatment of the mixed amalgam with sulphuric–acetic acid. The reduction of the acetate solution with sodium amalgam may be repeated till removal of europium is quantitative, but the first treatment gives the bulk of the europium at a concentration of 20—30%. Treatment of such a concentrate with cold dilute nitric acid results in selective oxidation of samarous sulphate and formation of samarium nitrate solution, which is then filtered from europous sulphate, but retained for reworking for a small amount of europium present in it.

The greater part of the europium is now sufficiently concentrated to apply McCoy's method of purification by precipitation as $EuCl_2,2H_2O$, but if the europium has not been through an amalgam stage at the first step, and thereby had all earths other than samarium removed, amalgam formation is advantageous now. The amalgam is then treated with concentrated hydrochloric acid and yields europium(II) chloride crystals and samarium(III) chloride solution.

It was observed that an acetate solution containing a trace of neodymium in much europium lost the neodymium absorption spectrum when the europium was reduced to the bivalent state on first being treated with sodium amalgam. When the europium had been extracted from the solution as amalgam with more sodium, the neodymium absorption spectrum reappeared. There is evidently an equilibrium, $Nd^{\cdots} + Eu^{\cdot\cdot} \rightleftharpoons Nd^{\cdot\cdot} + Eu^{\cdots}$, and $[Nd^{\cdot\cdot}][Eu^{\cdots}]/[Nd^{\cdots}][Eu^{\cdot\cdot}] = \text{const.}$ When $[Eu^{\cdot\cdot}]$ is large, a high proportion of neodymium will become bivalent. Conversely, as has been noted in previous Parts, the yields of amalgams are very adversely affected

by large amounts of non-reducing earths, so that it may be impossible to remove the last trace of a potentially bivalent material from admixture with them; *e.g.*, high [$Nd^{...}$] will stabilise small amounts of $Eu^{...}$, or high [$Lu^{...}$] small amounts of $Yb^{...}$ (Part III; this vol., p. 8). If the bivalent ion can be removed as rapidly as formed and before decomposition, *e.g.*, by precipitation as sulphate, then the more stable bivalent element may be removed from solution quantitatively, and with an efficiency varying with the insolubility of the sulphate. Since in the bivalent state the characteristic absorption bands of the rare-earths are lost, it follows that in concentrated bivalent solutions absorption-spectrum tests for traces of other earths become unreliable.

It has been noted in previous work that the bivalent ion of ytterbium or samarium is much more stable in neutral than in acid solution; *e.g.*, if the amalgams are treated with acid, at first only tervalent salts are formed, $2Sm^{..} + 2H^{\cdot} \longrightarrow 2Sm^{...} + H_2$; but as [$H^{\cdot}$] decreases, the colour of the bivalent ion develops in the solution. This is of interest in connection with the difficulty experienced in obtaining high-purity europium by repeated precipitations of its bivalent sulphate with magnesium sulphate (McCoy, *loc. cit.*). The europous solution stabilises quantities of the cerium earths in the bivalent state and they are then co-precipitated with the europium; but by precipitation of europous chloride with concentrated hydrochloric acid the equilibrium was altered so that nearly pure $EuCl_2,2H_2O$ was deposited. Bivalent europium alone possesses appreciable stability in strongly acid solutions.

Most of the present work has been done with artificial mixtures of europium and samarium containing 1% of the former, *i.e.*, a proportion of europium to samarium not more than that occurring in monazite. It is found that europium forms amalgams rather more readily than samarium, doubtless owing to the greater stability of the europous ion. Quantitative separation of europium can therefore be achieved without obtaining a fully quantitative samarium extraction. Conversely, from the mixed amalgam on attack by acetic acid, europium passes into solution relatively more quickly than samarium. This is in accord with the reduction potentials (Noddack and Brukl, *Angew. Chem.*, 1937, **50**, 362), *viz.*, $Sm^{..} \rightarrow Sm(metal) = -2{\cdot}010$ v.; $Eu^{..} \rightarrow Eu(metal) = -2{\cdot}510$ v. on the hydrogen scale for 0·01M-sulphate solutions. That europium amalgam is not always more reactive than samarium amalgam is shown by the fact that the former remains mirror-bright in open air for 10 minutes, and the latter for only a fraction of a second. The stability of europium amalgam in air affords an excellent indication of its purity.

The solubility of europous sulphate in saturated europium sulphate solution (*ca.* 30 g./l. of anhydrous salt) is 0·19 g./l., that of samarous sulphate being 0·075 g./l. (Holleck and Noddack, *ibid.*, p. 819). The solubilities are therefore of the same order as that of strontium sulphate in water (0·11 g./l.), and considerably greater than that of barium sulphate (0·0011 g./l.), but these sulphates are much more soluble in certain salt solutions. A study of europous sulphate in rare-earth chloride and acetate solutions has therefore been made, and shows it to be much more soluble in the chlorides than in the acetates. In the latter, the solubility is sufficiently small to allow an almost quantitative precipitation without the use of barium sulphate as co-precipitant, which McCoy found necessary when using chloride solutions. Moreover, the europium separation may be facilitated by co-precipitation of samarous sulphate. Samarium precipitation does not occur to any great extent in chloride solution, for the higher solubility and ionisation allow the samarous ion to reoxidise as quickly as it is formed. It is easy, however, to prepare samarous sulphate by acting on samarium amalgam with dilute sulphuric or acetic–sulphuric acid.

Several methods of separating samarium and europium on decomposition of the mixed amalgam (Eu/Sm = 1/100) have been tried.

(1) By allowing the amalgam to stand in contact with acetic acid containing a little sulphuric acid at room temperature for 18—20 hours, 50—60% of the europium was recovered as nearly pure sulphate (II).

(2) By carrying out the foregoing treatment in a hydrogen atmosphere, the yield was increased to over 90% of the europium.

(3) By acting on the amalgam with acetic and sulphuric acids at 65° in a hydrogen atmosphere with shaking, europous sulphate was recovered at a concentration of about 20%, accompanied by much samarous sulphate, but in nearly quantitative yield. The samarium sulphate was then oxidised and dissolved by cold dilute nitric acid, leaving the europous sulphate nearly unaffected and about 90% pure.

(4) Under the conditions of (3) but in the presence of a zinc salt, the bivalent sulphates are rendered less stable by the finely divided reduced zinc which is formed. According to the quantity of zinc, the formation of samarous sulphate may be restrained or the yield of bivalent sulphate may vanish. The action of dispersed metallic zinc in decomposing bivalent sulphate is similar to a phenomenon noted by the author (J., 1937, 1367), *viz.*, that traces of metallic salts in ytterbium sulphate solutions on electroreduction gave rise to a grey cloud which very much reduced the stability of the ytterbous sulphate. McCoy found lead to behave similarly in oxidising europous chloride. Even violent shaking, with consequent dispersion of mercury, may bring about the same result.

(5) If an acetate solution of samarium and europium is treated with zinc amalgam (2%) and a little sulphuric acid and kept acid with acetic acid while steam is blown through, a precipitate of mixed europous–samarous sulphate is formed and a concentrated samarium solution is left with a europium content of 0·02%. No samarous sulphate will be precipitated in the absence of europium. The reduction potentials for 0·01M-sulphate solutions have been determined by Noddack and Brukl (*loc. cit.*) as $Eu^{...} \rightarrow Eu^{..} = -0{\cdot}71$ v.; $Sm^{...} \rightarrow Sm^{..} = -1{\cdot}72$ v.

(6) When no more europium can be eliminated by method (3), if a little barium amalgam is added to the

reaction mixture, barium sulphate will be slowly precipitated and carry with it the last of the europium. The treatment with barium may be repeated as long as the precipitate is obtained in a filterable condition: in the absence of europium it becomes too fine to be retained.

(7) Pure samarium amalgam may be used as the reducing agent in the same way as sodium amalgam (method 8): it has the advantage of not introducing impurity.

(8) A perfect elimination of europium from samarium is made by treating the mixed acetates with dilute sodium amalgam and a little sulphuric acid. A good concentration of europous sulphate is effected at once. This method introduces some sodium acetate but has much in its favour: it is easy and certain. Successive crops of sulphates are taken till soon it is found that the crop is pure samarous sulphate, and the main bulk of samarium is free from europium.

A modification of McCoy's precipitation method for $EuCl_2,2H_2O$ allows of its application at europium concentrations below 70%. By acting on impure europium amalgam with concentrated hydrochloric acid, precipitates have been formed even in presence of 90% of samarium. The europium precipitation, however, is not quantitative, and the samarium chloride retains some 5% of europium. Samarium chloride will itself be precipitated if the concentration of hydrochloric acid becomes too high. One or two repetitions may be required to produce europium of the highest purity.

Experimental.

Estimation of Europium in Samarium.—Solutions were mixed and precipitated with oxalic acid, wherefrom samarium oxide standards with 3·3, 1, 0·33, 0·1, 0·033, 0·01, and 0·003% of europium oxide were prepared. Comparisons of other samarium oxide samples were made with the above from graphite arc spectrograms taken on a medium quartz-prism spectrograph and examined with the aid of a Hilger spectrocomparator. The two sensitive lines of europium at this dispersion are beset by samarium lines: Eu λ 4205·046 (intensity 200) by Sm 4205·361 (int. 8), and Eu 4129·735 (int. 150) by Sm 4129·987 (int. 10). The most suitable europium line for detection and comparison purposes was 3819·66 (int. 500). According to the Massachusetts Institute of Technology Tables, this should be beset by Sm 3819·678 (int. 10), but this samarium assignment appears to be in error.

Ease of (a) *Formation and* (b) *Decomposition of Samarium–Europium Amalgams.*—(a) Samarium acetate (23 g.) and europium acetate (0·23 g.) were treated in solution with sodium (5 g.) in mercury, and the bulk of the rare-earths exchanged into amalgam. Another 0·5 g. of sodium extracted a further quantity of rare earth (0·635 g. of oxide) which contained only 0·02% of europium oxide. A final extraction with 0·3 g. of sodium yielded 0·185 g. of samarium oxide free from europium. The residual acetate on recovery yielded 0·14 g. of samarium oxide free from europium but showing some gadolinium arc lines.

(b) Some mixed amalgam (Sm 99%, Eu 1%) was decomposed with dilute acetic acid. Samples of amalgam were withdrawn at five stages in the reaction, and their total earth content recovered. Arc spectra showed that the relative proportion of europium in the amalgam fell regularly from 1% at the start to nil near the end, *i.e.*, europium reacts preferentially to samarium.

The Solubility of Europous Sulphate.—(1) *In acetate solution.* A solution of samarium acetate (= 10 g. of oxide) in water (65 ml.) was heated in a flask in brine (107°) stirred by a jet of steam. Saturated liquid (2%) zinc amalgam (10 ml.), acetic acid (1 ml.), magnesium sulphate (1 g.), and europium acetate (= 20 mg. of oxide) were added. A slight orange precipitate soon formed. It was concluded that the solubility of europous sulphate was equivalent to 0·2 g./l. of oxide. The samarium acetate solution at no time held sufficient europous salt to give a definite bleaching action on litmus paper.

(2) *In chloride solution.* Samarium chloride solution with europium acetate equivalent to 0·1 g. of oxide under similar conditions gave no precipitate, but the solution bleached litmus readily. The solubility of europous sulphate in samarium chloride must exceed seven times that in samarium acetate.

Separation of Europium (1%) *from Samarium.*—The mixed amalgam was first prepared from mixed acetates. The following is typical of this preparation: The acetates (45·8 g. = 20 g. of oxide) were dissolved in boiling water (90 ml.) and shaken with 0·3% sodium amalgam in successive portions of 175, 25, and 25 ml., acetic acid (2—2·5 ml.) being added during the reaction to prevent formation of a basic precipitate. The remaining samarium acetate (= 1 g. of oxide) was recovered, and contained only a trace of europium. The amalgam was washed once by running through water and then decomposed by various methods.

(1) Amalgam (= 10 g. of oxide), water (100 ml.), acetic acid (12 ml.), and sulphuric acid (0·2 ml.) were left in a separating funnel; reaction was complete in 18 hours, and a layer of sulphate lay on the mercury. It yielded 65 mg. of oxide which gave on solution an absorption spectrum of europium in which only a trace of samarium was visible; hence, about 60% of the europium in the amalgam had been recovered.

(2) Amalgam (= 19·2 g. of oxide), water (200 ml.), acetic acid (25 ml.), and sulphuric acid (0·2 ml.) were placed in a separating funnel which was then closed with a Bunsen valve to maintain a hydrogen atmosphere and set aside for 20 hours. The initial temperature was 35°. During the first and the last hour the funnel was shaken a few times. A greyish-orange precipitate of bivalent sulphates, a little mercury, and a few crystals of samarium acetate were separated. The precipitate yielded 0·18 g. of oxide. Some sulphate adhered to the funnel walls; this with the acetate crystals yielded another 0·145 g. of oxides, mainly samarium. The 0·18 g. of oxide was made into 0·6 ml. of solution and examined in a 1-cm. layer. The samarium absorption spectrum was compared with a standard and indicated 20%. The arc spectrum of the 0·145 g. showed it to contain much more than 3% of europium, and the oxide from the samarium acetate filtrate showed 0·06% of europium oxide. Residual samarium (0·64 g. of oxide) in the mercury amalgam was found to contain 0·1% of europium. Hence, 94% of the europium input is found in the two concentrates (0·325 g.), and 6% in the remaining samarium oxide (18·3 g.).

(3) Amalgam (= 18 g. of oxide), boiling water (162 ml.), acetic acid (18 ml.), and sulphuric acid (0·2 ml.) were placed in a separating funnel as in (2). The initial temperature of 65° was maintained by the heat of the reaction till the amalgam was nearly exhausted. The funnel was continuously shaken, and two additions each of 1 ml. of 10% sulphuric acid made in the course of the reaction (25 mins.). The acetate solution was filtered with suction. The orange residue and precipitate adhering in the funnel yielded 0·91 g. of oxide. The residual samarium in the mercury amounted to 0·93 g. of oxide and contained 0·2% of europium. The samarium acetate filtrate (16 g. of oxide) contained only about 6 mg. of europium [see method (6) for its removal]; 97% of the europium was concentrated in 5% of the material in this one reaction.

(4) Method (3) was repeated but during the early part of the reaction 15 mg. of hydrated zinc sulphate were added

This at first restrained the formation of samarous sulphate. The total yield of oxides from precipitated sulphates was reduced to 0·62 g. The colour of the sulphates was duller. The sulphate residue was separated and treated with cold 2N-nitric acid; it reacted immediately with effervescence, leaving a pale buff residue, which was at once filtered off. The filtrate yielded 0·44 g. of oxide, mainly samarium, and the residue 0·18 g. of oxide, mainly europium. In another experiment, but with 33 times as much zinc sulphate, a heavy grey cloud was produced but no europium.

In the following methods, acetate solutions were treated directly with reducing agents, and amalgam formation did not play an essential part.

(5) The samarium acetate solution from which europium had been incompletely separated by method (1) was placed in a flask in a boiling brine bath (107°) with 10 ml. of saturated liquid zinc amalgam (2%), and steam was blown through it for ½ hour. An orange-red precipitate formed, yielding 170 mg. of oxide. The remaining samarium acetate contained 0·02% of europium.

(6) The samarium acetate solution after treatment by method (3) was at once treated at its b. p. with 1 ml. of saturated barium amalgam (0·04 g. of Ba) in 5 ml. of mercury. A coloured precipitate was formed, and filtered off. A second treatment gave a smaller precipitate, which became filterable after a short time. The precipitates were digested with nitric acid and yielded 25 and 13 mg. of oxide respectively. Both were mainly samarium but contained perhaps 10% of europium. After an interval the solution was treated with zinc amalgam and steam (method 5) without result. Four more treatments each with 2 ml. of barium amalgam were given. Filtration from the sulphate precipitates was difficult, and the yields of 20, 9, 12, and 6 mg. of rare-earth oxides include much samarium from the unwashed filter-papers. Contents of 10, 3, 2, and 0·2% of europium oxide, respectively, were found. No trace of europium was then detectable in the arc spectrum of the samarium acetate.

(7) Samarium acetate (45 g., 0·1% of Eu), water (200 ml.), and sulphuric acid (0·2 ml.) were treated with samarium amalgam (50 ml.) at 70—75°. A precipitate, at first white but later orange, was formed. More samarium amalgam and sulphuric acid were added, and crops (0·22, 0·10, and 0·03 g.) of oxide were obtained. These contained much europium. By starting with a europium-free samarium amalgam, it would appear that an increased quantity of europium-free samarium should be producible by this means without introducing any impurity.

(8) Samarium acetate (135 g.) in 450 ml. of solution at 60° and 50 ml. of mercury were treated with 0·5 ml. of sulphuric acid and 0·33 g. of sodium in 10 ml. of mercury. Two further portions of sodium were added before any precipitate was formed. A trace of zinc reduced the stability and yield until it was removed with the first precipitate. The reaction mixture was shaken gently (too vigorous shaking gave a precipitate which could not be efficiently filtered off, and a vigorous reaction also tended to emulsify small quantities of mercury which, like zinc, reduced the stability of the sulphate). Pure samarous sulphate precipitates appeared more stable than mixed samarous–europous precipitates. After the filtration, the acetate solution was reheated and returned to the mercury, more sodium amalgam and sulphuric acid added, and another crop of insoluble sulphates obtained. This procedure was repeated several times, as shown in the table. The colour of the first four crops was different from that of later ones. The former contained the bulk of the europium. All were converted into oxides. Arc spectroscopy showed a rapid falling off in europium content in the later crops, and complete absence in the last. Only a little samarium (0·66 g. of oxide) was found in the mercury

Fractionations from samarium acetate = 60 g. of oxide.

Na, g.	H_2SO_4, ml.	AcOH, ml.	$M''SO_4$, as g. of oxide.	Remarks.
1	0·5	—	0·12	Grey-brown, unstable; Zn
0·4	0·5	—	0·40	Rust colour; much Eu
1	0·5	—	1·29	Brick red; much Eu
0·4	—	0·3	0·27	Red; much Eu
0·4	0·5	1·0	1·25	Bright red; 5% Eu
0·4	0·5	—	1·59	,, 0·3% Eu
0·4	0·5	—	0·86	,, 0·003% Eu
0·4	—	—	0·07	,, no Eu
			5·05	

Sm_2O_3 (purified, Eu-free):
54·3 *ex* acetate solution
0·66 *ex* amalgam

at the conclusion, and this was europium-free. The bulk of the samarium acetate was recovered by crystallisation, and was readily separable from the more soluble sodium acetate with which it was now mixed. The sulphuric acid used (3 ml.) was sufficient to combine with at least 8 g. of oxide to produce mixed europous–samarous sulphate, whereas only 5 g. of oxide were so recovered. Some sulphuric and acetic acid underwent reduction, and a ginger-like odour was always noticeable.

Purification of Europium by Precipitation of $EuCl_2.2H_2O$.—(a) *Initial* Eu <99%. Europium oxide (20 g.) which had been reduced 6 times by amalgamated zinc and precipitated with magnesium sulphate was made into acetate and dissolved in water; sodium (11 g.) in amalgam was added in three portions, together with acetic acid (5 ml.) during the reaction. A green colour developed, but was lost after the last sodium extraction. A final extraction with 0·7 g. of sodium yielded 24 mg. of oxide, apparently good europium. Recovery of earths from the acetate mother-liquor amounted to 70 mg. Gadolinium, samarium and much europium were found in these by arc spectroscopy: the presence of neodymium, cerium, and praseodymium or terbium was also detected. The europium amalgam was washed once by passage through water. It reacted rapidly with air, indicating the presence of samarium, but not with water. It was then treated with concentrated hydrochloric acid in a separating funnel fitted with a Bunsen valve. 60 Ml. of acid were used at first, but produced a green solution. Another 40 ml. were added and the colour was lost through fuller precipitation. When the reaction was complete, the solution was cooled in an ice-bath and filtered. The filtrate yielded 0·8 g. of oxide, and washings of concentrated hydrochloric acid another 0·8 g. of oxide. Samarium arc lines but not absorption bands were easily seen in filtrate spectra. Amalgam made from the main crop of purified europium remained mirror-bright for 10 minutes in open air, in striking contrast to the behaviour of less pure amalgam or to that of samarium or ytterbium amalgam. The arc spectrum showed no certain indication of samarium, which is the last impurity to be removed after this second amalgam formation.

(b) *Highly impure europium material* (Sm 70%). The mixed amalgam was formed in the usual manner, and treated with concentrated hydrochloric acid (20 ml.). A precipitate was formed and showed on solution at most a doubtful trace of samarium absorption bands indicative of <0·025 g. of samaria in 0·61 g. of oxide. The filtrate yielded 1·28 g. of samaria; arc spectroscopy showed 3—10% of europium in this. The treatment had therefore recovered some 80%

of the original europium substantially pure. Treatment of some 10% europium material resulted in the recovery of two-thirds of it pure. It is possible to precipitate samarium chloride almost quantitatively with hydrochloric acid (saturated at 0°), but not to obtain a quantitative precipitation of europium(II) chloride by hydrochloric acid before samarium(III) chloride begins to precipitate if there is a large proportion of it present. Nevertheless, for europium preparations of more than 10% content the above process leads to a rapid concentration.

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143. *The Properties of Freshly Formed Surfaces. Part I. The Application of the Vibrating-jet Technique to Surface-tension Measurements on Mobile Liquids.*

By C. C. ADDISON.

The application of the vibrating-jet technique to surface-tension measurement has hitherto been restricted owing to practical difficulties and to the complex mathematical treatment required. A practical technique and simple mathematical treatment are described which enable the method to be more readily applied to the measurement of the surface tension of pure mobile liquids and to the study of adsorption at freshly formed surfaces. The method is applicable to liquids of widely different density, surface tension, and chemical nature, and the constants as defined are independent of temperature.

THE forces determining the distribution of surface-active solute molecules between the surface and the bulk of a solution do not normally require more than several seconds to bring the surface to a condition of stable equilibrium. For any given liquid medium the properties of the equilibrium surface depend upon the concentration and the structure of the absorbent molecules, and have been investigated for long-chain carbon compounds (Powney and Addison, *Trans. Faraday Soc.*, 1937, **33**, 1243 *et seq.*), dyes (Gibby and Addison, J., 1936, 119), and small molecules (Addison, *Nature*, 1939, **144**, 250, 783). The time taken for the establishment of equilibrium also varies with the structure of the surface-active molecule concerned, and is partly dependent upon the type of measurement employed. For instance, the establishment of a true capillary rise in a clean capillary tube is almost instantaneous, whereas (Powney and Addison, *Trans. Faraday Soc.*, 1938, **34**, 356) in the drop-weight method at least 12 seconds must be allowed for the formation of each drop in order to obtain equilibrium conditions.

Little information is available on the properties of freshly formed surfaces, to which surface-active molecules are in the process of migrating and where surface orientation is not fully completed. A knowledge of the properties of such surfaces has practical as well as academic significance, since in many detergent processes the operative surfaces are never sufficiently old for equilibrium to be established. In such processes the operative surface energy lies between two limits, the " static " and the " dynamic " surface tension. The latter term is used here to denote the tension at any given surface age below that at which equilibrium is established. Therefore, although the term surface tension (which is widely accepted as an abbreviation for equilibrium or static surface tension) has a significance alone, the term dynamic surface tension has no significance unless related directly to surface age.

Adam (" Physics and Chemistry of Surfaces," Oxford Univ. Press, 1930, p. 324) considers that any method for studying the development of surface equilibrium should be capable of operating at surface ages of the order of 10^{-4} sec. The study of dynamic surface tensions has been handicapped by the lack of a method capable of measuring the surface tension of a liquid at very low surface ages, which at the same time utilised readily available apparatus and lent itself to simple mathematical interpretation. The vibrating-jet method is particularly suited to dynamic studies, since it provides stationary waves bounded by a continually renewed surface, but it has been little used because of the difficulty of standardising the conditions for wave-length measurement, and because the mathematical treatment necessary has rendered the method almost prohibitive where large numbers of measurements are contemplated. The work now described represents an attempt to adapt this method to routine laboratory work, and to simplify the mathematical relationship between measured wave-length, flow rate, and surface tension; it is a necessary precursor to experiments, to be described later, in which the vibrating-jet technique has been applied to the study of freshly formed surfaces less than 1 second old, in order to assess the rates at which surface-active molecules migrate to a surface and to determine the factors controlling their subsequent orientation.

The fact that the cross-sectional form of a jet of liquid issuing from an unsymmetrical orifice will oscillate between that of the orifice and the circular, thus giving rise to a series of waves, was first observed by Bidone (" Expériences sur la Forme et sur la Direction des Veines et des Courans d'Eau lancés par diverses Ouvertures," 1854) and Magnus (*Pogg. Ann.*, 1855, 95), who worked with large orifices of various shapes. Only a very few waves were obtained, and the experiments served only as illustrations of the phenomenon. Neither author offered an explanation of the recurrent return of the jet to the original cross-sectional shape, and the fact that it was due to surface tension (or "capillary force ") was first suggested by Buff (*ibid.*, 1857, Bd. C). Rayleigh (*Proc. Roy. Soc.*, 1879, **29**, 71) developed a mathematical relationship connecting the surface tension with the wave-length and the jet velocity, and reported a series of experiments designed rather to illustrate the theory than to prove that it could be applied to practical measurements. Piccard (*Arch. Sci. phys. nat.*, 1890, **26**, 561) and Meyer (*Wied. Ann.*, 1898, **66**, 523) used the method for comparative measurements only. The jet amplitudes used were large, and the measurements cannot be used for the direct determination of surface tension.

Pederson (*Phil. Trans.*, 1907, *A*, **207**, 341) first developed an accurate practical technique, but ignored the variations in wave-length which invariably occur at the beginning of a jet even when a pure liquid is employed, and an accurate treatment of the method from both practical and theoretical aspects was first made by Bohr (*ibid.*, 1909, *A*, **209**, 281), who related the dimensions of the jet of water flowing from an elliptical orifice with the surface tension by a formula which took into account the inertia of the atmosphere surrounding the jet, the viscosity of the liquid, and the correction for changing amplitude of oscillation in the jet. The practical measurements were limited to pure water, but the result obtained (72·23 dynes/cm. at 20°) would seem to indicate that for water at least no other complicating factors play a major part. Bohr's technique was applied by Stocker (*Z. physikal. Chem.*, 1920, **94**, 149) to a range of aqueous inorganic salt solutions.

The method has thus been developed to give accurate results for single liquids where a constant wave-length obtains over a major part of the jet. The mathematical relationships involved have been deduced by predetermining the probable complicating factors, and introducing the appropriate correction. As with all dynamic methods, there can be no guarantee that a relationship deduced by this means and found to be correct for one liquid will be universally applicable. The drop-weight method, for instance, has received similar mathematical treatment, but in order to make the method universally applicable, Harkins and Brown (*J. Amer. Chem. Soc.*, 1919, **41**, 499) found it necessary to connect drop size and surface tension by purely empirical tables of figures deduced from many actual measurements over the full range of surface tension. From a study of the relationship between jet dimensions and known values of surface tension (giving due consideration to the mechanism by which any particular complicating factor influences the measurements), it has now been possible to formulate a simple relationship which enables the vibrating-jet technique to be applied to the measurement of a wide range of surface tensions and is capable of rapid and simple mathematical treatment. Although suitable for determinations on single pure liquids, the method also finds very ready application where changes in tension are more important than high accuracy in the values themselves.

Surface tensions calculated by the method given below deviate from the true value if the test liquid has a high viscosity, and the method is only applicable to liquids or solutions of such viscosity that the energy dissipation due to the damping of the vibrations is negligible over the length of the jet. True results are obtained at all viscosities below 0·02 c.g.s. unit, but deviations occur at higher viscosities. As all the dilute aqueous solutions used, and the majority of common organic liquids, fall inside this range, the viscosity limit imposes no undue restriction on the applicability of the method.

Experimental.

Apparatus.—The apparatus used is shown in Fig. 1. A 2-l. aspirator *A* was fitted with water manometer *M* and a fine capillary tube BB_1. This tube was coated with a film of vaselin where it passed through the rubber bung, so that it could be readily adjusted to any required position. The liquid under test was led from the tubulure down a glass tube *C*, and both *A* and *C* were fixed rigidly in position. The lower end of tube *C* was connected to the jet tube *D* by a small piece of rubber tubing so that *C* and *D* made glass-to-glass contact. The jet tube, which was about 10 cm. long, was clamped at about 10° to the horizontal, and a millimetre scale *E* was fixed immediately behind the jet so that the tip of tube *D* lay on the zero of the scale. By this means the part of the jet of liquid to be measured flowed horizontally in front of the scale, and could be measured directly. The liquid was received in vessel *F*, which carried a 50-ml. calibration mark on the narrow neck immediately above the bulb. The jet was illuminated by a striplight *G* (at least equal in length to the jet of liquid) placed horizontally over the jet.

Arrangement for constant flow of liquid. It was necessary to maintain a steady and constant flow of liquid over a period of several minutes for each determination. The jet is very sensitive to disturbances in the reservoir, and most of the standard types of constant-head equipment were unsuitable owing to a pulsing action which was reflected in the jet. Both Pederson (*loc. cit.*) and Bohr (*loc. cit.*) described arrangements based on the distribution of test liquid between several reservoirs, but these are applicable only when an unlimited supply of test liquid is available, and when only small amounts of liquid were available, Pederson had to determine wave-lengths under a falling head of pressure. In view of the almost direct proportionality between wave-length and flow rate, a perfectly constant flow rate is essential, as emphasised by the fact that true oscillation takes place over only part of the jet length and the selection of the appropriate section of the jet involves measurement over the full length: this is only possible under a constant head of pressure.

In the apparatus shown, the head of pressure (h) is equal to the vertical distance from *D* to the lower tip of *B* (*i.e.*, B_1) irrespective of the level of the liquid above B_1. If *B* has a large internal diameter, the bubbling of air from B_1 to replace liquid flowing from the aspirator gives rise to a regular pulsing of the jet stream, which prevents measurement of wave-lengths. Under these conditions the operative head of pressure fluctuates over a range equal to the diameter of each air bubble. As the internal diameter of *B* is reduced, the pulsing action diminishes; when the bore of *B* is sufficiently fine the air issues as a continuous stream of small bubbles and a steady jet stream is obtained. If the reservoir *A* is rigidly fixed so that it cannot transmit mechanical vibration to *D*, the jet stream is not influenced by disturbances on the surface of the liquid in *A*. The appropriate internal diameter of *B* depends on the order of flow rates used, and therefore on the cross-sectional area of orifice *D*; the tube used had an internal diameter of 0·06 cm.

The length of tube *C* was adjusted (for liquids of various densities) to give appropriate flow rates. As the resistance of the system is thereby altered, the jet velocity does not vary in proportion to $\sqrt{2gh}$ and the flow rate was measured directly in every case. The vessel *F* was used for this purpose, and the flow rate (ml./sec.) was measurable to an accuracy of approx. 0·2% by taking the time required for the liquid to rise to the 50 ml. mark on the neck. (A similar instrument, with unbent neck was used in conjunction with the vertical jet.) The flow rate was confirmed by measurements taken before and after the readings on the jet.

Dimensions of orifice tube. In order to obtain the maximum length of unbroken jet, it is necessary that the jet should perform a single vibration only and that turbulent flow should be minimised. Any orifice formed by drawing down a tube of larger cross-sectional area than the final orifice gives rise to exaggerated jet amplitude, with consequent shortening of the unbroken stream. The longest unbroken jet was obtained from an orifice formed by slight lateral compression of a piece of capillary tubing. By this means the liquid stream issues from an orifice whose cross-sectional area is the same as that throughout the body of the tube, and optimum conditions for stream-lined flow are obtained. The sharp-

ness of the orifice edge also has a pronounced effect on the stability of the jet. Any form of grinding damages this edge and the jet used in these experiments was prepared by first softening and slightly flattening the end of a piece of capillary tubing (approximately 0·20 cm. internal diameter) and then breaking off the end of this tube at such a position that the major/minor axis ratio of the orifice so formed was as small as possible consistently with the formation of visible waves. The ratio used was 1·25.

Measurement of Wave-lengths.—A section of the jet is shown diagrammatically in Fig. 2. The jet formed by an elliptical orifice can be regarded for present purposes as composed of interlocking lenses in alternate vertical and horizontal planes. The true "nodes" are at *A*, *B*, *C*, and *D*, where the cross-section passes through the circular form. However, the jet must pass from *A* to *C* before the cross-section completes one full oscillation, and this distance represents the wave-length λ. This can be measured directly by two methods.

FIG. 1.

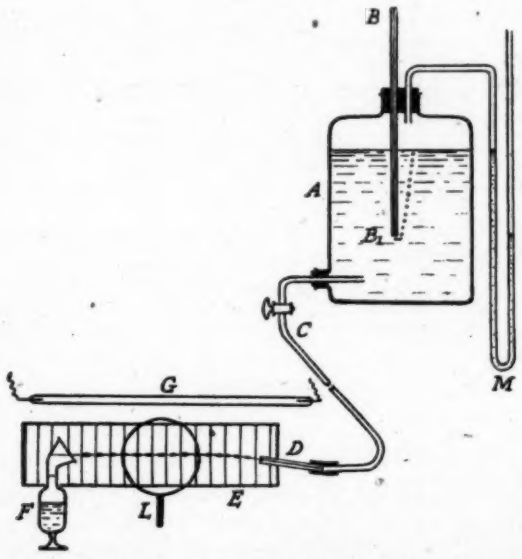
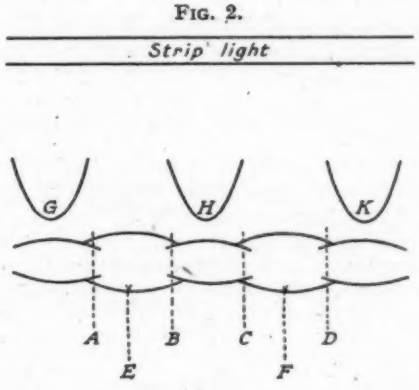


FIG. 2.



(a) *Large amplitudes.* When a striplight is placed vertically above the jet, and the jet is viewed in a horizontal plane, no reflection is seen in the horizontal lenses, but the lower boundary of the vertical lenses is outlined by a band of reflected light. As the light source is raised away from the jet, this strip of light is shortened, till eventually only a short narrow band remains on each vertical lens. The limits of this band are clearly defined, so the mean values (*i.e.*, points *E* and *F*) can be accurately determined. The distance *EF* is equal to *AC*, *i.e.*, the distance between successive bands of light represents one wave-length. By viewing the jet through a fixed lens *L* against a millimetre scale, the individual wave-lengths could be measured with an accuracy of 0·01 cm. The accuracy increases beyond this as the number of uniform waves available for measurement increases.

(b) *Small amplitudes.* As the amplitude of the jet decreases for any given wave-length, the accuracy of measurement by method (a) decreases because the length of the bright band of reflected light along the bottom edge of the vertical lenses cannot be sufficiently clarified and reduced. In certain positions of the light source, the rays of light are reflected and doubly refracted by the jet, and a wave image of exaggerated amplitude is thrown on the background scale. Pederson (*loc. cit.*) utilised this effect to throw images on to a photographic plate. The position of the image with respect to the jet is shown at *G*, *H*, and *K* in Fig. 2. The lowest point of each parabola of light corresponds exactly with the centre of a horizontal lens, and the distance between these points again represents the wave-length. As the amplitude of the wave image is many times greater than that of the jet itself, the accuracy is increased accordingly.

Temperature Measurement.—The temperature experiments were carried out by enclosing the whole apparatus in a large wooden box 2 ft. deep, kept by thermostat at approximately the required air temperature. The upper half of the front was formed of glass, and the lower part was open while the readings were being taken. Liquid at approximately the correct temperature was filled into the reservoir, and the liquid allowed to flow for a while before each determination to bring the apparatus to a constant temperature. The temperatures quoted in Table IV were obtained by allowing the jet to impinge directly on the bulb of a thermometer, and the arrangement described above was sufficient to prevent changes in temperature occurring during a determination.

DISCUSSION AND RESULTS.

Apart from the work of Satterly and Strachan (*Trans. Roy. Soc. Canada*, 1935, **29**, 105), who studied the vibrations which develop along a vertical jet of circular cross-section when the jet strikes a solid barrier, and some qualitative experiments by Rayleigh (*loc. cit.*), previous work in this field has been confined to the use of vibrating jets in a horizontal position. Although this renders unnecessary the application of correction factors for changing gravity effect along the jet, the use of a vertical jet offers pronounced practical advantages. The gravity effect in a horizontal jet, although uniform along the length of the jet, acts at right angles to the direction of flow. This force, being in the same plane as the two-dimensional oscillation, gradually upsets the purity of the vibrations, and quickens the break-up of the jet. Under identical reservoir conditions, the change in direction of the jet-tube from horizontal to vertical brings about an immediate increase of approximately 30% in the length of unbroken jet stream, with a corresponding increase in the range of surface ages available for measurement. Again, stable conditions for a pure liquid in a horizontal jet can be regarded as holding only

when the wave-length is constant along this jet. This is not necessarily true of the vertical jet, although the increase in wave-length due to the increasing velocity under gravity is largely compensated for by the decrease due to diminishing area of section.

The change in wave-length along the jet in both vertical and horizontal positions has been studied for distilled water at 20° at various flow rates. The results are shown graphically in Figs. 3 and 4, in which "wave

FIG. 3.

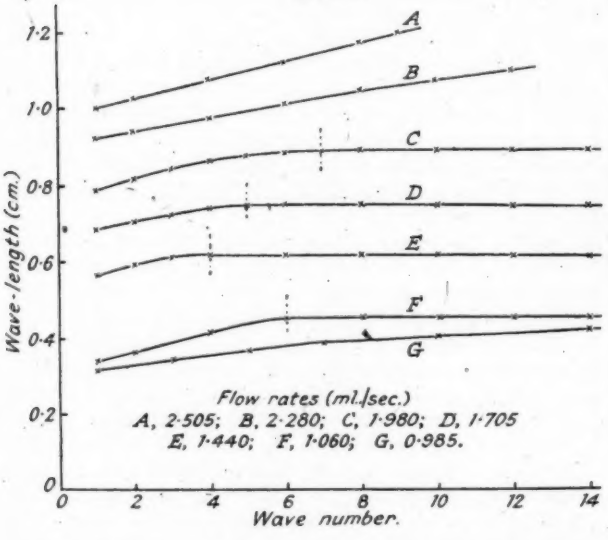
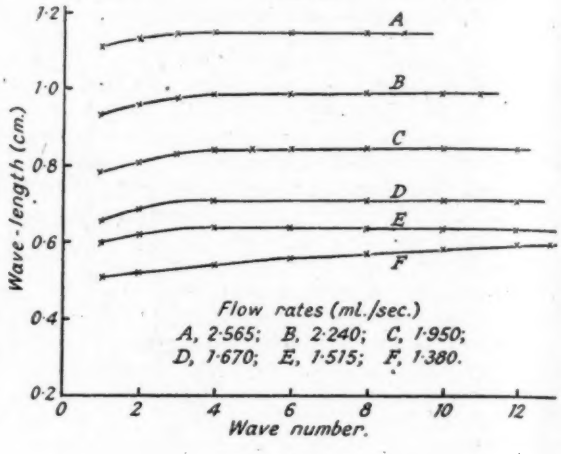
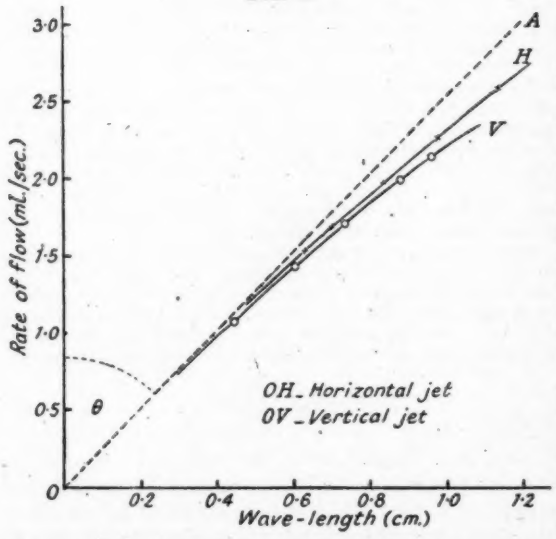


FIG. 4.



number" represents the serial number of the wave, counting along the jet from the orifice. In both cases the minimum flow rate for visible waves gives rise to a jet having a gradually increasing wave-length. In an ideal jet (in which the wave-length varies directly as the flow rate) the oscillations are two-dimensional, and this only holds true if the wave-lengths are considerable in comparison with the diameter of the jet. For small flow rates, either vertical or horizontal, the oscillations will be three-dimensional, and the oscillation frequency will depend upon the wave-length also. Again, the influence of gravity becomes more pronounced with a vertical jet as the flow rate increases, since the compensation due to decreasing jet radius is less and less able to counteract the increasing flow due to gravity. The vertical dotted lines in Fig. 3 indicate the position in the jet below which the wave-lengths are not constant, and their changing position along the jet is a measure of the relative predominance of these two effects. Even with the horizontal jet, however (Fig. 4), an increase in wave-length over the first four waves takes place irrespective of flow rate. Bohr (*loc. cit.*) observed this, and regarded it as being due to a difference between the rate of flow of liquid in the centre of the jet and at the surface, thus giving rise to a velocity potential which increases until balanced by the viscosity of the liquid. It is improbable that this cause alone is responsible, particularly as the wave-lengths have invariably been found to increase rather than decrease. No jet will be quite free from turbulent flow over its first few wave-lengths, and in view of the fact that the age of the surface at the end of the fourth wave-length is still less than 10^{-3} sec., the establishment of the true surface tension may also be partly responsible. Throughout this work it has therefore been necessary to ignore the first four wave-lengths as representing the period necessary for the establishment of fluid equilibrium.

FIG. 5.



The flow rate has been plotted against the equilibrium wave-length for both types of jet in Fig. 5. Although curves of similar type are obtained in each case, yet the gravity effect in the vertical jet results in a greater wave-length over the full range of flow rates. The surface tension of the liquid under test can be deduced from either of the two curves *OH* or *OV*. The mathematical treatment given below is applicable to horizontal jets only. However, where it is of advantage to obtain the maximum length of unbroken jet, a further gravity

factor can be superimposed to make the method applicable to vertical jets, and this will be the subject of a later part.

Curve *OH* in Fig. 5 indicates that the wave-length λ increases more rapidly than the flow rate, f. The time of oscillation (which in an ideal jet is independent of flow rate) therefore increases as flow rate increases. This effect has been found to occur in all liquids tested, and has been attributed by Rayleigh and Bohr to (*a*) the damping effect on the oscillations caused by the viscosity of the liquid, (*b*) the increasing magnitude of wave amplitudes which occurs with increasing flow rate, and (*c*) the inertia of the air phase. It is considered here that with liquids of low viscosity the velocity gradient set up at the orifice will be maintained throughout the jet, and will represent a further factor accounting in part for the disproportionate extension of wave-length which occurs. The restoring force (*i.e.*, surface tension, γ) acting on a particle on the surface of the jet will normally act at 90° to the direction of flow in the absence of a velocity gradient. A velocity gradient extending from the centre to the surface of the jet will cause the force γ to act at an angle of $90° + \alpha°$ to the direction of flow. As α will be small, $\tan \alpha$ will vary in proportion to the flow rate f. Although the point on the equivalent circle about which the particle oscillates is not quite at the centre of the amplitude, it is sufficiently near in the case of the small amplitudes used for the oscillation of the particle (mass m) to approach simple harmonic. The time of oscillation t (secs.) will then be given by

$$t = C(m/\gamma \cos \alpha)^{\frac{1}{2}} = C_1/(\cos \alpha)^{\frac{1}{2}}$$

where C and C_1 are constants. Now, since $tf = C_2\lambda$, then $f = \lambda C_3(\cos \alpha)^{\frac{1}{2}}$. This relationship between f and λ is the equation of a curve of the type shown in Fig. 5, but in the absence of a suitable practical method for determining the angle α and the velocity gradient, it is not yet possible to apply this equation quantitatively.

Relation between Wave-length, Flow Rate, and Surface Tension.—Rayleigh (*loc. cit.*) has shown that for an ideal jet, the expression for the time of oscillation takes the general form $t = K_1(dr^3/\gamma)^{\frac{1}{2}}$, where d is the density of the liquid and r the radius (in cm.) of the jet where its cross-section is circular; if λ is expressed in cm. and f in ml./sec., then $t = \pi r^2\lambda/f$, whence

$$\gamma = (K_1^2/\pi^2 r)d(f/\lambda)^2.$$

The value of r is that of the jet, not the orifice. Although there are reasons for believing that the extension of wave-length at the beginning of the jet is due to factors other than a change in linear velocity (with consequent reduction in jet radius), yet the assumption that the radius of a circle equivalent to the orifice can be used for r is not justified. As the apparatus is to be calibrated by using liquids of known surface tension, the term r can conveniently be incorporated in the constant in the above equation. Again, the value of λ/f for an ideal jet and any liquid is given by the slope of the tangent to the λ–f curve (Fig. 5) at the origin and can thus be replaced by $\tan \theta$. Hence

$$\gamma = K_2 d/\tan^2 \theta \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

θ has, of course, no significance as an angle, and is significant only when referred directly to its tangent; $\tan \theta$ for water was found by accurate construction to be 0·400 at 20°. By substituting the values $\gamma = 72{\cdot}8$ dynes/cm. and $d = 0{\cdot}9982$ at 20°, we find $K_2 = 11{\cdot}68$. This value varies, of course, with the jet used, but when once determined by this means, K_2 is a fixed property of the apparatus. Results given below indicate that K_2 is constant for all liquids tested, and is independent of temperature.

Determination of $\tan \theta$.—The large number of measurements required before $\tan \theta$ can be obtained by geometrical construction prohibits the use of this method for routine measurements, and where changes in wave-length occur along the jet, the method is not possible. It is therefore essential to obtain $\tan \theta$ from a single measurement of λ and f. The lower range of flow rates over which λ–f proportionality holds varies with the size of orifice and the nature of the liquid, but even in limiting cases where the departure from proportionality is just negligible the flow rate is still so small that a constant wave-length is not obtained even with pure liquids. Again, true two-dimensional oscillations do not operate until the flow rate is so large that the wave-length is appreciably affected by the factors mentioned above. There are therefore no practical conditions under which $\tan \theta$ can be obtained as the direct ratio of measured values of λ and f; it can, however, be obtained as follows.

When referred to its tangent *OA* as ordinate, the equation for curve *OH* (Fig. 5) has the general form $y^n = K_3x$. When referred to flow rate (f) and wave-length (λ) axes, the equation for the curve becomes

$$(\lambda \sin \theta + f \cos \theta)^n = K_3(\lambda \cos \theta - f \sin \theta) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where θ is the angle between the tangent and the f axis. Throughout this work $\tan \theta$ is related to f in ml./sec. and λ in cm. The flow rate f is expressed in volume rather than linear units to avoid reference to the accurate radius of the jet. The value of $\tan \theta$ for water (0·400) was substituted in the above equation in order to determine appropriate values for K_3 and n. Table I shows that as the wave-length increases the value to be given to n in order to maintain K_3 constant changes from 3 to 2, which is consistent with the change from three- to two-dimensional oscillation which takes place as the wave-length increases with respect to jet diameter. The table also indicates that for accurate determinations the ratio wave-length/jet diameter should be above 10 in order that true two-dimensional oscillation can operate.

TABLE I.

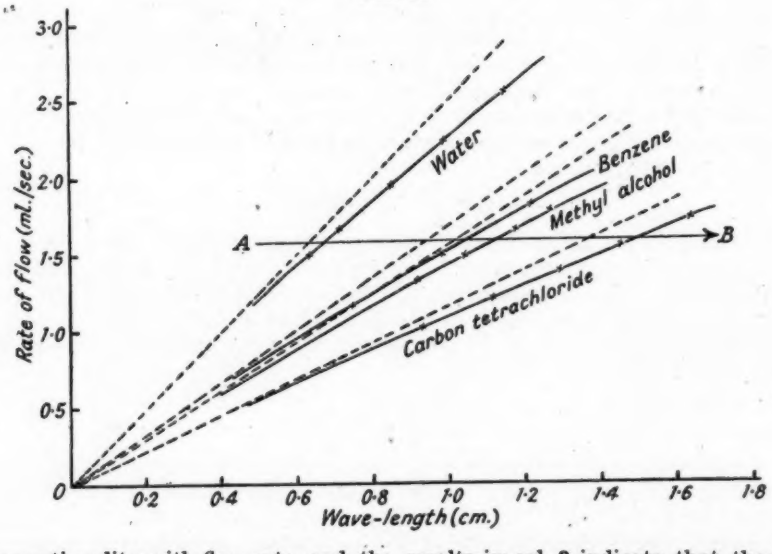
λ, cm.	0·640	0·714	0·850	0·990	1·150
f, ml./sec.	1·515	1·670	1·950	2·240	2·565
K_3, assuming $n = 2$	87·3	79·2	68·8	68·8	68·5
K_3, assuming $n = 3$	143	143	146	168	192
Approx. ratio, λ/jet diameter	8	9	10	12	14

With the apparatus used, therefore, the relationship between λ, f, and θ for water is

$$(\lambda \sin \theta + f \cos \theta)^2 = 68{\cdot}7\ (\lambda \cos \theta - f \sin \theta).$$

Variation of K_3 *with Properties of Liquid under Test.*—The relationship expressed in equation (1) provides a suitable means of determining the variations which occur in K_3 when equation (2) is applied to various liquids. Fig. 6 shows the relation between λ and f for benzene, carbon tetrachloride, and methyl alcohol under the same experimental conditions. The curve for water is reproduced for comparison. The known values for the surface tension being assumed, the value of θ was calculated for each of the three liquids from equation (1). This value was substituted in equation (2), with $n = 2$, and the values obtained for K_3 compared against K_3 for water, three separate values of λ and f being used in each case. The results are given in Table II, where K_4 is defined by $K_3 = K_4 d/\tan \theta$. The value of K_3 is a measure of the extent to which the wave-length departs

FIG. 6.



from the ideal proportionality with flow rate, and the results in col. 3 indicate that there are considerable variations from liquid to liquid.

TABLE II.

γ, cm.	f, ml./sec.	K_3.	K_3/d.	K_4.	γ, cm.	f, ml./sec.	K_3.	K_3/d.	K_4.
H_2O; γ used = 72·8 dynes/cm. at 20°; tan θ = 0·400.					CCl_4; γ used = 26·7 dynes/cm. at 20°; tan θ = 0·835.				
1·150	2·565	68·5	68·6	27·5	1·728	1·875	51·8	32·4	27·6
0·990	2·240	68·8	68·8	27·6	1·606	1·750	51·4	32·2	27·4
0·850	1·950	68·8	69·0	27·6	1·422	1·570	51·9	32·6	27·8
C_6H_6; γ used = 28·9 dynes/cm. at 20°; tan θ = 0·596.					MeOH; γ used = 22·6 dynes/cm. at 20°; tan θ = 0·640.				
1·220	1·820	40·9	46·6	27·8	1·312	1·790	34·8	43·9	27·9
0·980	1·495	41·1	46·8	27·9	1·206	1·660	34·4	43·5	27·5
0·800	1·240	41·5	47·3	28·2	1·062	1·480	34·0	42·9	27·3

As the period of oscillation in a jet is a direct function of the density of the liquid, the deviations from ideal behaviour must also vary with density. The values of K_3/d are therefore listed in col. 4. These represent the true basis on which to compare the various liquids, and again they vary considerably from liquid to liquid.

The broken-line tangents in Fig. 6 represent the ideal λ–f ratio for each of the four liquids. The major causes of deviation from these lines, *i.e.*, air-phase inertia, velocity gradient, viscosity potential, and variations in wave amplitude, are each functions of the flow rate, and their influence upon wave-length must necessarily depend upon the frequency of vibration. As the wave-length increases for any given flow rate (say, along the line AB in Fig. 6) the rate of oscillation decreases and the factors causing deviation will play a less significant part. It was therefore to be expected that the value K_3/d would decrease with increase in tan θ. The respective values given in Table II show that, in fact, a clear inverse proportionality exists, and that if K_3 in equation (2) be replaced by $K_4 d/\tan \theta$ the value of K_4 is constant for all four liquids.

Determination of Surface Tension of any Liquid.—The results set out above indicate the probability that

surface tension values for any liquid can be determined by the following method: (1) Accurate determination of wave-length and flow rate. (2) Substitution of these results in the expression: $(\lambda \sin\theta + f\cos\theta)^2 - K_4 d\,(\lambda\cos\theta - f\sin\theta)/\tan\theta$. (The value K_4 depends upon the dimensions of the apparatus used and can be obtained as shown above.) (3) K_4, d, λ, and f being known, it is possible to find the value of θ at which the expression has zero value. This is readily done by substituting into the expression two near values of θ, plotting the values obtained for the expression against the angle, and reading off the value of θ; $\tan\theta$ then has direct significance in terms of wave-length per unit flow rate. (4) Substitution of the value of $\tan\theta$ so obtained in the expression $\gamma = K_3 d/\tan^2\theta$.

This simple procedure, which had so far been shown to give true surface-tension values for four liquids of widely different density, surface tension, and chemical nature, was then applied to the determination of the surface tensions of other liquids. The results are given in Table III and are in good agreement with results obtained by other methods.

TABLE III.

Liquid.	λ, cm.	*f*, ml./sec.	tan θ.	γ, dynes/cm. at 20°.	Liquid.	λ, cm.	*f*, ml./sec.	tan θ.	γ, dynes/cm. at 20°.
Et_2O	1·320	1·640	0·700	17·0	$CHCl_3$	1·480	1·690	0·801	27·2
C_7H_{14}	1·060	1·495	0·630	20·1	PhMe	1·206	1·815	0·595	28·5
EtOH	1·060	1·480	0·640	22·5	*m*-$C_6H_4Me_2$ ...	1·000	1·510	0·594	28·7
$COMe_2$	1·104	1·580	0·620	23·8					

Influence of Temperature.—Surface-tension measurements have been made for four liquids over a range of temperature, in order to verify that the method and constants which have been shown to give satisfactory results at 20° are applicable over the range of temperature required. The flow rates chosen were such that at the lowest temperature the wave-lengths were still sufficiently long to ensure pure two-dimensional vibration. The results are given in Table IV. The height of the capillary air inlet *B* into the reservoir was adjusted at each temperature so that the flow rate was constant throughout the tests on any one liquid. Thus the variation of wave-length with temperature is immediately available from Table IV.

TABLE IV.

Liquid.	Temp.	*f*, ml./sec.	λ, cm.	tan θ.	γ, dynes/cm.	$-d\gamma/dt$.
H_2O	13°	2·025	0·874	0·398	73·8	0·150
	33	2·025	0·900	0·406	70·6	0·160
	45	2·025	0·916	0·410	68·7	0·166
	60	2·025	0·940	0·417	66·0	0·180
CCl_4	7	1·620	1·432	0·816	28·3	0·120
	32	1·620	1·520	0·854	25·1	0·135
	48	1·620	1·580	0·884	23·0	0·140
C_6H_6	11	1·690	1·106	0·587	30·0	0·120
	35	1·690	1·180	0·611	27·0	0·130
	50	1·690	1·240	0·630	24·9	0·140
MeOH	8	1·715	1·214	0·628	23·8	0·080
	18	1·715	1·238	0·635	23·0	0·085
	38·5	1·715	1·304	0·656	21·0	0·105
	50	1·715	1·340	0·671	19·8	0·115

Thermal agitation in the jet was responsible for a progressive shortening of the unbroken jet as temperature increased. It was possible in each case to shorten the jet to less than 5 waves, and the highest temperature recorded in Table IV represents the limit to which the temperature could be raised without reducing the unbroken jet to less than 5 waves.

The results obtained indicate that the method can be applied over a range of temperature, and that the constants as defined are independent of temperature.

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144. *The Course of Autoxidation Reactions in Polyisoprenes and Allied Compounds. Part VII. Rearrangement of Double Bonds during Autoxidation.*

By E. HAROLD FARMER, H. P. KOCH, and DONALD A. SUTTON.

Ethyl linolenate and methyl docosahexaenoate, both displaying unsaturation of the methylene-interrupted type, ·C:C·C·C:C·C·C:C·, are shown by spectrographic measurements to develop conjugated diene and conjugated triene unsaturation during the incorporation of molecular oxygen. The extent of double bond displacement is correlated with the degree of peroxidation occurring. Squalene and rubber, both displaying a different type of unsaturation, ·C:C·C·C·C:C·C·C·C:C·, do not similarly develop conjugated units. The mechanism of autoxidative reaction in the two cases is discussed.

In Part V (this vol., p. 122) it was reported that a typical drying-oil ester, methyl docosahexaenoate, showed a marked increase in its capacity to absorb ultra-violet light as the result of exposure to atmospheric oxygen in the illumination of the laboratory. The rapid peroxidation of the polyene system which set in during this

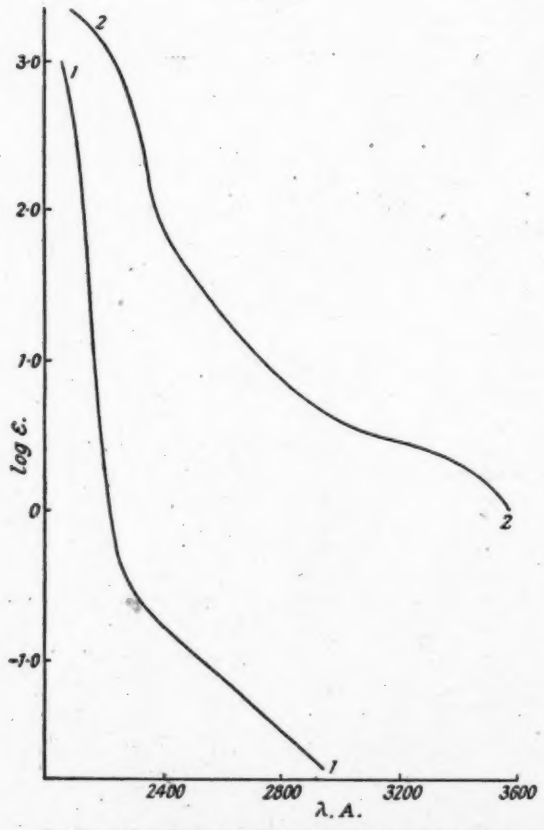
exposure promoted a structural change apparently of a conjugative nature. The nature of this change is now examined. Two types of unconjugated unsaturation are, however, taken into consideration, (1) the methylene-interrupted unsaturation, ·C:C·C·C:C·C·C:C·, characteristic of numerous unconjugated drying-oil acids such as linoleic, linolenic, and various polyene fish-oil acids, and (2) the more widely spaced unsaturation found in rubber and in other unconjugated polyisoprene hydrocarbons. The structural changes that ensue on oxidation are of particular interest in relation to the free-radical mechanism of olefinic peroxidation already formulated (Farmer, Bloomfield, Sundralingam, and Sutton, *Trans. Faraday Soc.*, 1942, **38**, 348) in which the olefin is regarded as passing through the stages :

$$\cdot CH\cdot C:C\cdot \longrightarrow \cdot C\cdot C:C\cdot \longrightarrow \cdot \underset{\displaystyle OO^{*}}{\overset{|}{C}}\cdot C:C\cdot \longrightarrow \cdot \underset{\displaystyle OOH}{\overset{|}{C}}\cdot C:C\cdot$$

the asterisk representing the radical centre.

Materials.—For the purpose of differentiating quite clearly the effect of oxidation from that of (*a*) thermal treatment (cf. forthcoming paper) and (*b*) alkali treatment (cf. Farmer, *Trans. Faraday Soc.*, 1942, **38**, 357), it has been necessary to work with materials as nearly as possible spectroscopically pure. For this reason subjection of the materials during their preparation to temperatures above 115°, to prolonged treatment with alkali, or to the action of atmospheric oxygen was highly undesirable. Ethyl linolenate represented a favourable case for study, the only undesirable feature attending its preparation being the necessity to subject the parent linseed oil to a short saponification with alkali. Methyl docosahexaenoate, which was selected to represent the unconjugated polyene esters derived from fish oils, had also to be submitted to short treatment with alkali at the first stage of its preparation, but the use of high temperatures, and exposure to oxygen during its laborious isolation were altogether avoided by a modification of Farmer and Van den Heuvel's original method (*J. Soc. Chem. Ind.*, 1938, **57**, 24). The yellow colour of the fish-oil ester, which developed rapidly in the

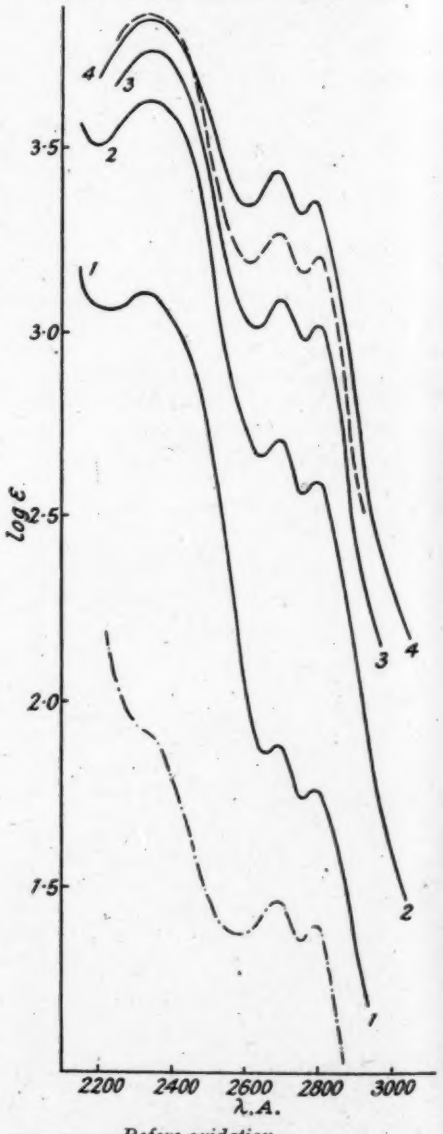
FIG. 1.



Spectra of cyclo*hexene* (1) *and* cyclo*hexene hydroperoxide* (2) *in* cyclo*hexane.*

FIG. 2.

Spectra of ethyl linolenate (in ethanol).



—·—·—·— *Before oxidation.*
—·——·— *After* 1·2% (1), 3·9% (2), 6·5% (3), *and* 11% (4) *oxidation.*
– – – – – *After* 8·5% *oxidation in dark.*

presence of oxygen, could only be completely removed by chromatographic treatment of the ester with alumina in an atmosphere of purified nitrogen. Squalene and rubber were employed to exemplify the second type of unsaturation. The former was rectified by molecular distillation below 112°, and then further purified by chromatographic treatment in purified nitrogen, and the latter was freed almost entirely from impurities by fractional dissolution of crepe rubber in petroleum–acetone in an atmosphere of nitrogen (Bloomfield and Farmer, *Trans. Inst. Rubber Ind.*, 1940, **16**, 69).

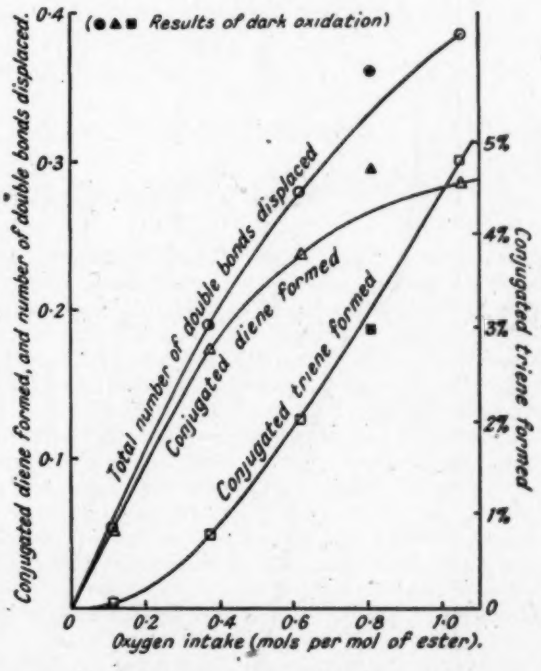
Spectrographic Examination of Autoxidised Materials.—In determining the structural cause of the strong light-absorbing capacity of the autoxidised fish-oil ester, it was necessary at the outset to gain information concerning the peroxide chromophore. This has been examined in detail, and it is found that the strong light-absorption in the regions of 2400 and 2700 A. is not to be attributed to the peroxido-olefin structure but must be associated with the formation of conjugated groups by double-bond shift in the carbon chain during its oxygenation. The spectrum of a typical olefin peroxide is compared with that of the parent olefin in Fig. 1. The most interesting features are the widely increased general absorption and the new broad band beyond 3000 A., but the extinction values are low throughout the ultra-violet range. Simple alkyl peroxides appear to be even more transparent (Lederle and Rieche, *Ber.*, 1929, **62**, 2573), so the influence of peroxidic absorption can certainly be neglected in the presence of typical organic chromophores.

Spectrographic analysis of the early stages of atmospheric oxidation of ethyl linolenate,

$CHEt{:}CH{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH{:}CH{\cdot}[CH_2]_7{\cdot}CO_2Et$,

during which all the incorporated oxygen survives in peroxidic form, has revealed the emergence of intense selective absorption in two well-defined wave-length regions (cf. Fig. 2). In the absence of any possible chromophoric oxygen groups, maximum absorption near 2340 A. is known to characterise the spectrum of a straight-chain conjugated diene (cf. spectrum of alkali-isomerised linoleic acid according to Mitchell, Kraybill, and Zscheile, *Ind. Eng. Chem. Anal.*, 1943, **15**, 1), and the two narrow bands at 2690 and 2800 A. are typical of straight-chain conjugated trienes such as elæostearic acid or alkali-isomerised linolenic acid (van der Hulst, *Rec. Trav. chim.*, 1935, **54**, 639; Mitchell *et al.*, *loc. cit.*). The starting material (dotted curve, Fig. 2) evidently contains traces of similar absorbing compounds as impurities.

Fig. 3.



Assuming maximum molecular extinction coefficients of 24,400 and 47,300 for ethyl-alcoholic solutions of pure conjugated diene and triene respectively (figures calculated from the data of Mitchell *et al.*), and allowing for irrelevant absorption at 2690 A. due to the ascending branch of the short-wave band at 2340 A., we can estimate the actual amounts of conjugated material produced from ethyl linolenate during autoxidation. In Fig. 3 the number of conjugated diene groups per mol. of ester and the percentage concentration of conjugated triene formed are plotted against the observed intake of oxygen. It can be seen that, after the incorporation of 1 mol. of oxygen, rearrangement of double bonds has progressed to a stage at which *ca.* 28·5% of the ester taken contains two double bonds in conjugation, and 4·5% has all three double bonds conjugated. The top curve of Fig. 3 represents the total number of double bonds displaced, account being taken of the fact that two double bonds must be shifted for each conjugated triene system formed. The initial slope of this curve shows that during the early stages of autoxidation each molecule of oxygen absorbed is 50% effective in moving one double bond into conjugation.

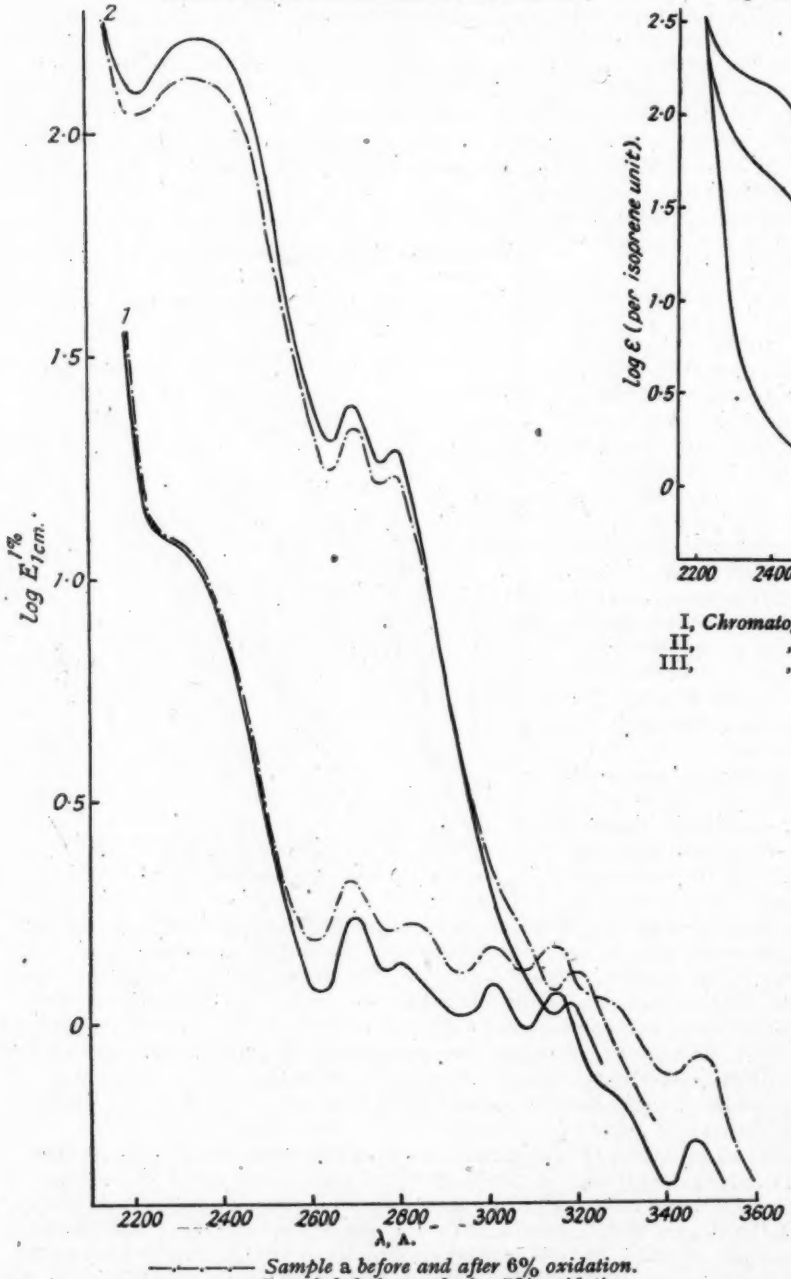
The absorption spectra of two samples of methyl docosahexaenoate were also examined before and after autoxidation, and the occurrence of the same process of double-bond rearrangement during oxidation is revealed by the development of intense absorption in the originally feebly absorbing regions of 2340 and 2700 A. (Fig. 4). The bands near 3015, 3165, 3290, and 3480 A. exhibited by the unoxidised ester were also observed by Edisbury, Morton, and Lovern (*Biochem. J.*, 1935, **29**, 899) in all their samples of fish-oil acids and are doubtless due to the presence of traces of higher conjugated polyenes. An important effect of autoxidation is the destruction of these conjugated systems implied by the decreased absorption at longer wave-lengths. The new band at 3190 A. is probably associated with the triene spectrum (van der Hulst, *loc. cit.*).

The rearrangement phenomenon was overlooked by Treibs (*Ber.*, 1942, **75**, 925), who studied the course of autoxidation of linoleic, linolenic, and liver-oil hexaene esters refractometrically; he found that there is no exaltation of the molecular refraction which could be ascribed to conjugated unsaturation after the incorporation of 1 mol. of oxygen. This finding agrees with our own observations on autoxidised methyl docosa-

hexaenoate (cf. Part V, *loc. cit.*), but in our experience the original ester always showed an exaltation of *ca.* 1 unit, which disappeared as autoxidation (accompanied by rapid increase in the density and comparatively slow increase in the refractive index) proceeded.* Refractivity measurements are clearly unreliable as a guide to the presence of conjugation in the highly autoxidisable substances displaying methylene-interrupted unsaturation.

FIG. 4.

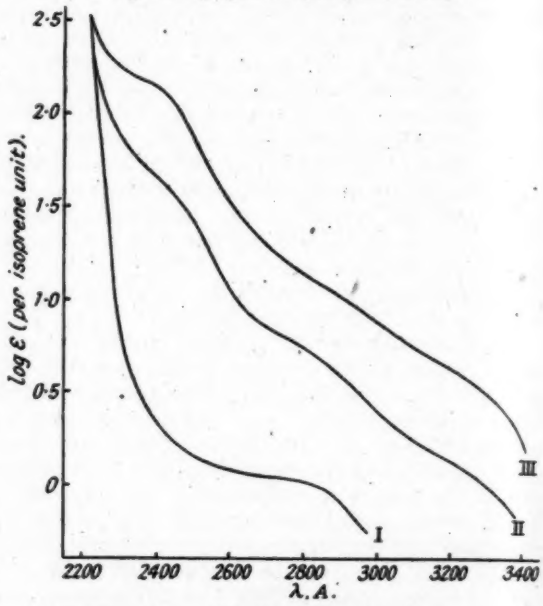
Spectra of methyl docosahexaenoate (in ethanol).



—·—·—·— *Sample* a *before and after* 6% *oxidation.*
——— *Sample* b *before and after* 7% *oxidation.*

FIG. 5.

Spectra of squalene (in cyclohexane).



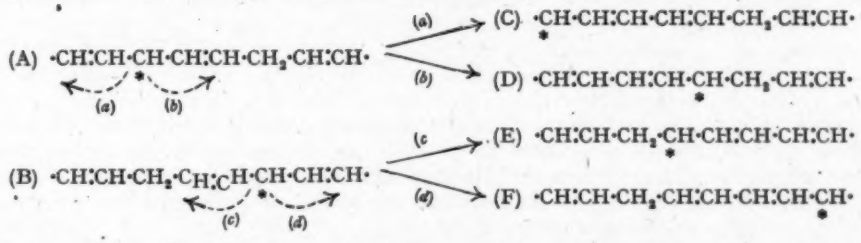
I, *Chromatographically purified squalene.*
II, ,, *after* 3·7% *U.V. oxidation.*
III, ,, *after* 9% *U.V. oxidation.*

In contrast to the foregoing, when solutions of carefully purified squalene and of fractionated rubber were similarly examined before and after autoxidation, no strong increase in the absorption of light which could definitely be ascribed to the formation of conjugated units was observed. The spectra for squalene and two

* An early normal value of $[R_L]_D$ reported by Farmer and Van den Heuvel (J., 1938, 429) was due to unsuspected oxidation of the distilled ester.

of its oxidation products (3·7% and 9% oxygen-intake) are represented in Fig. 5. The small increases in absorption there shown may be due to small degrees of conjugation, or to the formation of peroxide groups (cf. the effect on light absorption of peroxide groups in the case of *cyclo*hexene), or to a combination of both.

Course of Conjugative Change.—If the first stage of peroxidation consists in the severance (presumably by the aid of molecular oxygen) of a thermally or photochemically activated α-methylenic C–H bond, so leaving an olefinic free *radical*, it may be expected that resonance between the two 3-carbon forms $\cdot\overset{3}{C}H{:}\overset{2}{C}H\cdot\overset{1}{C}H\cdot$ and $\cdot\overset{3}{C}H\cdot\overset{2}{C}H{:}\overset{1}{C}H\cdot$ will immediately follow, so that when in succession a molecule of oxygen and an atom of hydrogen (the latter probably detached from a nearby molecule) come to be incorporated, there will be an approximately equal tendency for the ·OOH group to appear at the positions 1 and 3, and for the double bond to remain at the original position or to appear at the adjacent C–C bond. In the methylene-interrupted type of unsaturation considered above, the most reactive methylene groups are those flanked on either side by a double bond, and if the two methylene groups of this type in ethyl linolenate were to be attacked singly by oxygen the original radical forms (A) and (B) would be supplemented by (C)—(F) :



The hydroperoxides derived from (C)—(F) would then show diene conjugation. Similarly if *both* the reactive methylene groups were attacked consecutively by oxygen, which would happen frequently only in advanced stages of oxidation, then five other (di-)peroxido-forms would become possible, three of which would show diene conjugation, one triene conjugation, and the last the original state of unconjugation. Now if on each occasion that a hydrogen atom is detached from just one of the active methylene groups of a linolenic molecule the tendency for the radical centre so formed to migrate to left or right is assumed to be about equal to the tendency for it to retain its original position, then it will follow that only half the radical molecules that are ultimately successful in combining with oxygen and hydrogen to give mono-hydroperoxido-compounds will yield conjugated forms; if, however, all of the three resonance forms derivable by loss of a hydrogen atom from a pentadiene system ·CH:CH·CH₂·CH:CH· are to be regarded as possessing equal stability, the proportion of conjugated to unconjugated forms will rise to *ca.* 2 : 1. Since the hydroperoxido-derivatives of ethyl linolenate undergo little decomposition during the absorption of the first molecule of oxygen by the ester, the quantitative relationship between the conjugated and the unconjugated forms produced is likely to have remained substantially unchanged by secondary reaction in the present experiments: the product, however, at the end of the "monoperoxidation" stage is likely to have contained diperoxido- and unchanged ester molecules as well as monoperoxido-derivatives.

In the case of the polyisoprene hydrocarbons, however, the reactive α-methylene groups are flanked only on one side by double bonds. This leads in practice to a much lower reactivity of the olefin, and, in terms of the hypothesis, to the necessity for two successful peroxidations to occur in any unconjugated diene unit of the chain (C:C·C·C·C:C) before diene conjugation can appear therein. Furthermore, the hydroperoxide groups formed in these compounds are very unstable, so that no very high (overall) percentage of peroxidic oxygen survives at the end of an experiment, and this applies whether the oxidation is restricted to an early stage or whether it is carried (in ultra-violet light) to an advanced stage; also the decomposition of the peroxide groups leads to a corresponding degree of destruction of unsaturation. It is not surprising, therefore, that in practice peroxidation does not produce any considerable degree of conjugation. The occurrence, however, of peroxidation at all in rubber, squalene, etc., may well cause change in the original arrangement of the double bonds, and so contribute to the observed heterogeneity of the final oxidation products, *e.g.*,

$$\cdot CMe{:}CH\cdot CH_2\cdot CH_2\cdot CMe{:}CH\cdot \longrightarrow \cdot CMe{:}CH\cdot CH_2\cdot CH{:}CMe\cdot CH(OOH)\cdot \text{ or } \cdot CMe(OOH)\cdot CH{:}CH\cdot CH_2\cdot CMe{:}CH.$$

Presumably the easily oxidisable forms displaying methylene-interrupted unsaturation which ought thus to be produced by the first double-bond shift do not accumulate sufficiently in the earlier stages of autoxidation to cause by their further oxidation appreciable change in the direction of conjugation over the whole material; also in the more advanced stages where their numbers should increase their effect is nullified by the destruction of unsaturation accompanying peroxide decay.

If the free-radical mechanism of autoxidation is the correct one, double-bond shifts appear not unlikely to occur also in the autoxidation of mono-olefinic substances, since the 3-carbon grouping $\cdot\overset{3}{C}H{:}\overset{2}{C}H\cdot\overset{1}{C}H\cdot$ is concerned here also, so that methyl oleate should give the peroxido-forms $\cdot C_{11}{:}C_{10}\cdot C_9(OOH)\cdot C_8$ and $\cdot C_{11}\cdot C_{10}(OOH)\cdot C_9{:}C_8\cdot$ as well as $\cdot C_{11}(OOH)\cdot C_{10}{:}C_9\cdot C_8\cdot$ and $\cdot C_{11}\cdot C_{10}{:}C_9\cdot C_8(OOH)$. This deduction has not been

tested experimentally, but the fully hydrogenated derivatives of hydroperoxido-oleic acid which were described in Part IV may well include 9- and 10-, as well as 8- and 12-hydroxystearic acid. In addition, since the production of conjugated forms from the above-mentioned substances has never been observed to occur in the entire absence of oxygen, even after many hours of illumination in ultra-violet light, the further deduction can hardly be resisted that molecular oxygen (in spite of various recorded observations to the effect that the rate of autoxidative reaction in olefins is independent of the oxygen concentration) plays a direct part in detaching sufficient hydrogen atoms * from the α-methylenic C–H bonds to initiate the necessary reaction chains for bringing about successful autoxidation.

No distinction has hitherto been made in this series between the course of photochemical and that of thermal oxidation, since not only have experimental conditions in which both thermal and photochemical activation are possible usually been employed, but no results pointing to the functioning of two different mechanisms of oxygen incorporation have yet been obtained. It is now found that, apart from the induction period (see below), the result of conducting an oxidation of ethyl linolenate at room temperature in complete darkness is exactly the same with regard to efficiency of peroxide formation and the extent of double bond rearrangement as that obtained in (summer) daylight. The dotted curve in Fig. 2 represents the absorption spectrum of this thermally oxidised ethyl linolenate (8·5% oxygen uptake), and the three black points in Fig. 3 the extent of conjugation and the total double-bond shift produced by the oxidation. The free-radical mechanism of peroxidation, therefore, appears to apply to thermal as well as to photo-oxidation. It is of interest also that the analogy formerly pointed out by one of us (Farmer, *Trans. Faraday Soc.*, 1942, **38**, 340) between the mechanism of olefinic autoxidation and that of maleic anhydride addition to olefins at high temperatures clearly needs to be extended to include double-bond shifts in the latter reaction exactly comparable with those reported above to occur in the former. Alder (*Ber.*, 1943, **76**, 27) has recently observed that both maleic anhydride and azodicarboxylic esters unite with allylbenzene to give adducts of the type $CHPh{:}CH{\cdot}CH_2R$ (not $CHPhR{\cdot}CH{:}CH_2$), R representing the maleic or azodicarboxylic grouping, and similar results obtained by one of us will be published later.

Experimental.

cyclo*Hexene*.—*cyclo*Hexene was purified for optical examination by the method of Stücklen, Thayer, and Willis (*J. Amer. Chem. Soc.*, 1940, **62**, 1717), who record, over the range examined by them, an absorption curve identical with that given in Fig. 1.

cyclo*Hexene Peroxide*.—This was prepared by Farmer and Sundralingam's method (J., 1942, 132) and twice distilled at 27°/0·03 mm. for spectrographic examination. Further distillation of the sample caused no change in the absorption curve.

Ethyl Linolenate.—Hexabromostearic acid (m. p. 185°) was debrominated according to Norris, Kass, and Burr (*Oil and Soap*, 1940, **17**, 123), and the resultant crude ester molecularly distilled at 78° (Found: C, 78·3; H, 11·3; I.V., 246. Calc. for $C_{20}H_{34}O_2$: C, 78·4; H, 11·2%; I.V. for $|\overline{3}$ 249). The ester was kept sealed in a vacuum until required for use, and its absorption spectrum determined within 40 mins. of opening the tube.

Autoxidation.—Since no water is eliminated during the early stages of oxygenation (Farmer and Sutton, *loc. cit.*; Treibs, *Ber.*, 1942, **75**, 203), the oxygen intake was determined by direct weighing against a tare. Small beakers (2 cm. diameter) containing about 200 mg. each of the ester were exposed during June to a dust-free atmosphere at 20° ± 3° near a window facing north. At intervals, successive samples were re-weighed, made up to a known volume in ethyl alcohol, and immediately used for spectrographic and peroxide determination, the latter by the method of Bolland *et al.* (*Trans. Inst. Rubber Ind.*, 1941, **16**, 29). The observations were completed within 2 hrs. of re-weighing. It was found that 1·1% of oxygen (P.O.C., 1·3%) was absorbed in 24 hrs., 3·7% (P.O.C., 4·1%) in 48 hrs., 6·3% (P.O.C., 6·7%) in 72 hrs., and 12·0% (P.O.C., 10·3%) in 110 hrs. In the dark, no oxygen was absorbed by the ester during the first 2 days, but 8·7% (P.O.C., 8·1%) was found to be absorbed after 7 days.

Methyl Docosahexaenoate.—The glycerides of cod-liver oil of good quality were converted by the action of methanolic hydrogen chloride into the corresponding methyl esters. From the mixed esters a fraction judged to contain the whole of the C_{23}-ester fraction was separated by a series of molecular distillations at temperatures below 115°. This fraction, containing some saturated and possibly some mono-olefinic esters in addition to the polyene esters, was *rapidly* saponified with a small excess of methanolic potassium hydroxide, and the potassium soaps converted *via* the free acid into the corresponding lithium soaps. By fractional crystallisation of the latter from acetone, the (relatively soluble) lithium soap of the crude hexaene acid was segregated, and thereafter converted *via* the free acid into the corresponding methyl ester. This was finally fractionated by molecular distillation. All operations were conducted in an atmosphere of purified nitrogen or in high vacuum. Two samples were employed: (*a*) one fraction distilled at 91° which still contained traces of the C_{21} ester ($|\overline{5}$), and (*b*) another at 110° which gave satisfactory analytical values for the C_{23} ester ($|\overline{6}$).

Autoxidation.—The oxidation technique was essentially similar to that outlined above. Sample (*a*) absorbed 6·3% (P.O.C., 5·8%) of oxygen in 72 hrs., and sample (*b*) (under rather more favourable conditions) 7·2% (P.O.C., 6·9%) in 28 hrs.

Squalene.—Portions of the purified squalene (Found: C, 87·85; H, 12·35. Calc. for $C_{30}H_{50}$: C, 87·72; H, 12·28%) were shaken (without solvent) with oxygen in ultra-violet light at *ca.* 35° until (*a*) *ca.* 3·5% and (*b*) *ca.* 9% of oxygen had been absorbed. The two products had: (*a*) C, 84·5; H, 11·85; O (diff.), 3·65; P.O.C., 1·7%, and (*b*) C, 79·8; H, 11·25; O (diff.), 8·95; P.O.C., 3·54%.

Rubber.—A sample of purified rubber, dissolved in spectroscopically pure *cyclo*hexane, was shaken with oxygen at *ca.* 35° in ultra-violet light until *ca.* 1% of oxygen had been absorbed. The product had: C, 87·2; H, 11·75; O (diff.), 1·05%.

Spectrographic Measurements.—The Spekker photometer was used in conjunction with a tungsten-steel spark and a Hilger Small Spectrograph E 484 which gives a dispersion of 30 A./mm. at 2700 A. and 20 A./mm. at 2340 A. Spectral photographs exhibiting a high degree of contrast were obtained on Kodak B-10 plates. Two concentrations of ester solution normally sufficed to cover the entire range of the spectrum when two different cell lengths were used. *cyclo-*

* Probably in the form of HOO* radicals. Kinetic studies of the course of reaction will be published later by the authors' colleagues.

Hexane and ethyl alcohol were specially purified for absorption measurements (Twyman and Allsopp, " Absorption Spectrophotometry," p. 67).

The above work has been carried out as part of a programme of fundamental research on rubber undertaken by the Board of the British Rubber Producers' Research Association.

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[*Received, August 13th,* 1943.]

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145. *The Synthetic Application of* o-β-*Bromoethylbenzyl Bromide. Part II. The Preparation and Properties of* 2-*Substituted* 1 : 2 : 3 : 4-*Tetrahydroisoarsinolines.*

By FREDERICK G. HOLLIMAN and FREDERICK G. MANN.

By the Michaelis condensation of *o*-β-bromoethylbenzyl bromide with phenyl- and methyl-dichloroarsine in the presence of metallic sodium and ethyl acetate, 2-*phenyl*- and 2-*methyl*-1 : 2 : 3 : 4-*tetrahydroisoarsinoline* have been prepared. This novel heterocyclic system proved to have considerable stability, and the spontaneous fission of the heterocyclic ring shown by the quaternary methiodide of 1-methyl-1 : 2 : 3 : 4-tetrahydroarsinoline in solution does not occur with the *iso*arsinoline analogues. A number of derivatives of the *iso*arsinolines have been prepared, but none of the compounds tested possessed trypanocidal or antimalarial activity.

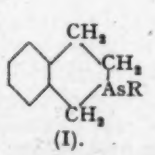
o-β-BROMOETHYLBENZYL bromide is now readily available (Holliman and Mann, J., 1942, 737) and we are investigating its use in the synthesis of various heterocyclic systems. It is known to condense with primary amines to give 2-substituted 1 : 2 : 3 : 4-tetrahydro*iso*quinolines, and consequently we have investigated first its utilisation for the preparation of derivatives of the unknown 1 : 2 : 3 : 4-tetrahydro*iso*arsinoline.

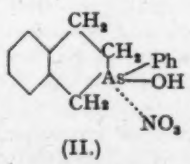
In preliminary experiments, we attempted to prepare a " double Grignard " reagent by the interaction of the dibromo-compound with 2 equivs. of magnesium, with the intention of subsequently treating this reagent with, *e.g.*, phenyldichloroarsine. Since, however, all attempts to prepare this Grignard reagent proved unsatisfactory, we had recourse to the Michaelis reaction, and treated an ethereal solution of the bromide and the dichloroarsine directly with metallic sodium. Very little reaction occurred even in the boiling solution until a small quantity of ethyl acetate was added; this caused a brisk reaction to ensue, and, provided oxygen was carefully excluded throughout the preparation, distillation of the final solution gave 2-*phenyl*-1 : 2 : 3 : 4-*tetrahydroisoarsinoline* (I; R = Ph) as a colourless liquid, b. p. 128—130°/0·05 mm.

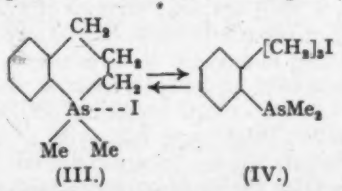
This arsine showed many of the normal properties of a tertiary arsine: *e.g.*, with methyl iodide it gave a quaternary *methiodide*, and with nitric acid it gave the characteristic and highly crystalline *hydroxy-nitrate* (II). This can clearly be regarded as a salt of the *iso*arsinoline oxide or the corresponding dihydroxide, but neither of these oxy-compounds could be isolated in the pure crystalline state. The *iso*arsinoline in chloroform solution readily absorbed one mol. of bromine to give the arsine dibromide, which, however, when treated with aqueous ammonia furnished ultimately only a colourless glassy product; this was obviously the oxide or dihydroxide, since with nitric acid it gave the hydroxy-nitrate, and with alcoholic hydrogen chloride the *arsine dichloride.*

It has been shown by Mann (J., 1932, 958) and Mann and Chaplin (J., 1936, 527) that tertiary arsines react with chloramine-T to give either an arsinimine, $R_3As{\rightarrow}N{\cdot}SO_2{\cdot}C_6H_4Me$, or the corresponding hydroxysulphonamide, $R_3As(OH){\cdot}NH{\cdot}SO_2{\cdot}C_6H_4Me$, the direction of the reaction being determined by the nature of the groups R. The phenyl*iso*arsinoline (I; R = Ph) reacted readily with anhydrous chloramine-T in absolute alcohol, but only an amorphous glass was isolated; this, when treated with water, gave toluene-*p*-sulphonamide, and the aqueous extract must therefore have contained the arsine oxide or dihydroxide: again, however, all attempts to isolate these compounds failed, but their presence in the solution was clearly shown by the fact that addition of nitric acid gave the hydroxy-nitrate, and picric acid precipitated the crystalline *hydroxy-picrate.* In contrast to this failure to isolate the oxide, the corresponding iso*arsinoline sulphide* was readily obtained as a highly crystalline solid by the interaction of the *iso*arsinoline dibromide and hydrogen sulphide.

A Michaelis condensation between *o*-β-bromoethylbenzyl bromide, sodium, and methyldichloroarsine, when also stimulated by ethyl acetate, similarly gave 2-*methyl*-1 : 2 : 3 : 4-*tetrahydroisoarsinoline* (I; R = Me), a liquid of b. p. 131°/18 mm., which was more susceptible to atmospheric oxidation than the phenyl analogue.


(I).


(II.)


(III.) (IV.)

It formed a crystalline *methiodide*; oxidation with nitric acid did not, however, give a crystalline oxide or hydroxy-nitrate, but the aqueous solution of the product readily furnished a crystalline *hydroxy-picrate.*

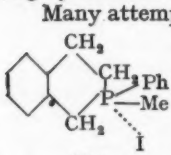
Chloramine-T reacted with the methyl*iso*arsinoline, giving only a viscous syrup, which on treatment with water gave toluene-*p*-sulphonamide, the aqueous extract again furnishing with picric acid the *iso*arsinoline hydroxy-picrate. The methyl*iso*arsinoline, unlike its phenyl analogue, failed to form a crystalline sulphide.

The methyl*iso*arsinoline is of particular interest because it is isomeric with the 1-methyl-1 : 2 : 3 : 4-tetrahydroarsinoline first prepared by Burrows and Turner (J., 1921, **119**, 430) and further investigated by Roberts, Turner, and Bury (J., 1926, 1443). They adduced evidence that the methiodide (III) of their compound underwent partial ring fission in alcoholic solution, and thus existed in equilibrium with *o*-(γ-iodo-*n*-propyl)phenyldimethylarsine (IV). The establishment of this equilibrium was indicated by the fact that the cold colourless solution of (III) on warming became yellow, but on cooling again became colourless: strong evidence of the equilibrium, however, was obtained from the fact that a rapid estimation of ionic iodine in the cold alcoholic solution always gave low values.

We at first suspected that a similar equilibrium occurred in alcoholic solutions of the quaternary iodides of our tetrahydro*iso*arsinolines. It was noteworthy that the methiodide of (I; R = Ph) was markedly more soluble in cold alcohol than that of (I, R = Me); moreover, the former gave a faintly yellow solution even in cold alcohol. Further evidence showed, however, that the tetrahydro*iso*arsinoline ring system must have great stability and it is unlikely that any such ring fission in solution occurs. Estimation of ionic iodine in our two methiodides, even when carried out as rapidly as possible in cold solution, always showed complete ionisation of iodine present; moreover, the isolation of optically stable quaternary salts of (I; R = Ph) (see following paper) would have been impossible had any such equilibrium arising from ring fission occurred. It is concluded that the pale yellow colour of alcoholic solutions of the methiodide of (I; R = Ph) probably arose from slight photochemical decomposition.

The methyl*iso*arsinoline readily united with chlorine in carbon tetrachloride solution to give the *arsine dichloride*, which on heating lost methyl chloride and generated *2-chloro*-1 : 2 : 3 : 4-*tetrahydro*iso*arsinoline* (I; R = Cl). By boiling this compound with pyridine, we attempted to remove hydrogen chloride and thus prepare 3 : 4-dihydro*iso*arsinoline, but there was no appreciable change. Roberts, Turner, and Bury (*loc. cit.*) record a similar failure to remove hydrogen chloride from 1-chloro-1 : 2 : 3 : 4-tetrahydroarsinoline by the action of diethylaniline. These failures are not unexpected for theoretical reasons. The tetrahydro-arsinolines and -*iso*arsinolines are presumably stabilised by "buckling" of the reduced arsine ring; the completely unreduced compounds—if they could be isolated—would undoubtedly be stabilised by resonance: the intermediate dihydro-compounds possess neither of these stabilising factors in full measure and hence are apparently highly unstable.

Many attempts were made to prepare *2-phenyl*-1 : 2 : 3 : 4-*tetrahydro*iso*phosphinoline* by a Michaelis reaction between *o*-β-bromoethylbenzyl bromide, sodium, and phenyldichlorophosphine. The reaction in ether or in benzene, with or without ethyl acetate, failed to give any satisfactory distillate; the addition of antimony chloride as a catalyst (see Worrall, *J. Amer. Chem. Soc.*, 1930, **52**, 2933) was without apparent effect in our experiments. The reaction in ether using ethyl acetate did give a very small distillate, which evidently contained the required phosphinoline in an impure condition, since treatment with methyl iodide ultimately gave the pure crystalline *methiodide* (V).



(V.)

Similar attempts to prepare the corresponding *iso*stibinoline also failed, no definite product being obtained when phenyldi-iodostibine was used in the Michaelis condensation, in spite of wide variation in the conditions employed.

In view of the novel character of the tetrahydro*iso*arsinoline derivatives, they have been examined for possible therapeutic activity of various types. Dr. G. Brownlee, of the Wellcome Physiological Research Laboratories, has compared the compounds (I; R = Ph), (II), and (I; R = Me) and its methiodide with neoarsphenamine for their ability to protect from death mice infected with lethal inocula of *Trypanosoma equiperdum*: for this purpose, the substances were administered (*a*) suspended in gum acacia and given by mouth, (*b*) suspended in olive oil and injected intraperitoneally, (*c*) mixed in propylene glycol and similarly injected, (*d*) emulsified in Lanette wax and similarly injected. He has also compared (II) and the above methiodide in 0·2% aqueous solutions with neoarsphenamine for their ability to protect mice similarly infected, the compounds being administered by the tail-vein in doses of 0·16 mg./20 g. mouse, each test being carried out with a group of 10 mice. All tests gave negative results, and the compounds are apparently devoid of trypanocidal activity.

Dr. Ann Bishop, of the Molteno Institute of Parasitology, has also tested (II) and both methiodides [from (I; R = Ph or Me)] against infections of *Plasmodium relictum* induced in canaries by inoculation with infected blood: none of the compounds showed any significant antimalarial action.

Dr. E. Baldwin and Dr. E. Friedmann, of the Cambridge University Biochemical Laboratory, have also tested (II) in 0·05% aqueous solution on isolated pieces of pig *Ascaris*, but these were unaffected.

General considerations, based on active drugs which also contain heterocyclic systems, would indicate that the marked therapeutic inactivity of these *iso*arsinoline compounds is probably closely associated with the unsubstituted benzene ring, and that the introduction of amino-, chloro-, or ethoxy-groups into this ring might render the compounds physiologically active. The introduction of such groups into the original *o*-β-bromoethylbenzyl bromide is exceedingly difficult, in view of the various stages in its synthesis. Consequently, such groups would have to be inserted in the final tetrahydro*iso*arsinoline molecule, *e.g.*, by direct

nitration followed by replacement of the nitro-group by the desired substituent; but sufficient quantities of the *iso*arsinolines are not yet available for experiments on these lines.

Experimental.

2-Phenyl-1 : 2 : 3 : 4-tetrahydroisoarsinoline (I; R = Ph).—A solution of *o*-β-bromoethylbenzyl bromide (50 g.) in dry ether (750 c.c.) was prepared in a 1500-c.c. round-bottomed flask fitted with a 3-neck adaptor which carried a reflux water-condenser, a dropping funnel, and an inlet tube by which a current of nitrogen could be passed through the apparatus. Phenyldichloroarsine (40 g., 1 mol.) and fine sodium wire (35 g., 8·3 atoms) were added, the air displaced by dry nitrogen, and ethyl acetate (5 c.c.) finally added. The mixture was refluxed for 6 hours, ethyl acetate (5 c.c.) again added, and the refluxing continued for a further 3 hours, by which time the sodium wire had completely disintegrated and a heavy brown precipitate had formed in the brown solution. A slow current of nitrogen was passed into the flask throughout these operations. The reflux condenser was now replaced by a glass ∩-tube, one limb of which reached to the extreme bottom of the reaction flask, and the other led through a cork which securely closed the top of a sintered-glass filter-funnel, the stem of which was fitted in turn into the main neck of a 50-c.c. Claisen distilling flask. The latter carried a condenser fitted with a rotating series of receivers. It was thus possible by means of the compressed nitrogen (or carbon dioxide) to force the ethereal solution of the arsine slowly over into the sintered filter, and allow the filtrate to enter the distilling flask without exposure to oxidation; the ether was meanwhile gently distilled off, so that ultimately the distilling flask contained the whole of the crude arsine. The latter was now distilled under reduced pressure, and a main fraction, b. p. 156—162°/0·4 mm., collected: this on refractionation gave the pure *isoarsinoline* (I; R = Ph), b. p. 110—112°/0·01 mm., 128—130°/0·05 mm.; yield 12·8 g. (31·5%) (Found: C, 66·1; H, 5·6. $C_{15}H_{15}As$ requires C, 66·7; H, 5·6%).

Methiodide. A mixture of the *iso*arsinoline and excess of methyl iodide was refluxed for 30 mins., the unchanged iodide then allowed to evaporate spontaneously, and the dark oily residue dissolved in a small quantity of ethyl alcohol and set aside. Crystallisation started after several days and was increased by cautious addition of ether. The crystals were collected, and redissolved in alcohol, from which the pure colourless *methiodide* slowly separated, m. p. 136—137° [Found: C, 46·9; H, 4·6; ionic I, 30·2; I (Carius), 31·5. $C_{16}H_{18}IAs$ requires C, 46·6; H, 4·4; I, 30·8%]. The ionic iodine was estimated by dissolving the iodide (*ca.* 0·4 g.) in cold 95% alcohol (200 c.c.), adding 40% aqueous silver nitrate solution (1 c.c.) containing 2 or 3 drops of concentrated nitric acid, shaking the mixture for 2—3 mins., and then without delay collecting the silver iodide in a Gooch crucible in the usual manner.

Oxidation of (I; R = Ph).—(a) *With nitric acid.* The *iso*arsinoline (1 g.) was just covered with water, and concentrated nitric acid (2—3 c.c.) added; oxidation and heat evolution occurred, and the oily product rapidly solidified on cooling and stirring. Two recrystallisations from dilute aqueous nitric acid gave the colourless crystalline *hydroxy-nitrate* (II), m. p. 149—150° (Found: C, 51·7; H, 4·4; N, 4·1. $C_{15}H_{16}O_4NAs$ requires C, 51·6; H, 4·6; N, 4·0%).

(b) *With bromine.* A cooled solution of the *iso*arsinoline (1·32 g.) in chloroform (30 c.c.) was treated with a solution (7·5 c.c.) of bromine in chloroform (10·63 g./100 c.c.), *i.e.*, with 1 mol. of bromine. The bromine was at once absorbed, and the colourless solution was then shaken with excess of dilute aqueous ammonia. The aqueous layer was separated and evaporated to dryness, the residue extracted with chloroform, and the united chloroform extracts evaporated. The hygroscopic glassy residue could not be crystallised, but its identity as the arsine oxide or dihydroxide was shown by two experiments. (i) A solution of a portion of the residue in hot water was treated with nitric acid, and the above hydroxy-nitrate crystallised on cooling; after recrystallisation from dilute nitric acid, it had m. p. and mixed m. p. 149—150°. (ii) A solution of another portion in hot alcohol was saturated with hydrogen chloride; on cooling, colourless crystals of the *isoarsinoline dichloride* separated, which, after recrystallisation from alcoholic hydrochloric acid, had m. p. 147—149° (Found: Cl, 19·9. $C_{15}H_{15}Cl_2As$ requires Cl, 20·8%). This dichloride, when treated with water and nitric acid, again furnished the hydroxy-nitrate.

(c) *With chloramine-T.* Anhydrous chloramine-T (1·5 g.) was added to a solution of the *iso*arsinoline (1·7 g., 1 mol.) in absolute alcohol (30 c.c.), heat being immediately evolved and sodium chloride precipitated. The mixture was refluxed for 5 mins., filtered, and the cold filtrate evaporated in a desiccator at room temperature. The residual glass could not be recrystallised from any anhydrous solvent. On trituration with water, toluene-*p*-sulphonamide separated (m. p. after recrystallisation from benzene, 136—137°, mixed and unmixed): the presence of the arsine oxide or dihydroxide in the aqueous extract was shown by two experiments. (i) A portion of the extract, treated with nitric acid, gave the hydroxy-nitrate, m. p. 149—150° (Found: N, 4·0%). (ii) Another portion, when treated with saturated aqueous picric acid solution, gave an emulsion: addition of alcohol to the heated mixture then gave a clear solution, which on cooling deposited the *hydroxy-picrate*, m. p. 116—118° after recrystallisation from alcohol (Found: C, 48·7; H, 3·8; N, 8·4. $C_{21}H_{18}O_9N_3As$ requires C, 48·9; H, 3·5; N, 8·15%).

2-Phenyl-1 : 2 : 3 : 4-tetrahydroisoarsinoline Sulphide.—Hydrogen sulphide was passed for 30 mins. into a chilled solution of the arsine dibromide in chloroform prepared as above. The solution was filtered from traces of sulphur and evaporated on the water-bath; the oily residue, diluted with alcohol, readily gave the solid *sulphide*, which crystallised from alcohol in colourless needles, m. p. 124° (Found: C, 60·1; H, 5·3; S, 10·7; *M*, ebullioscopic in 1·23% alcoholic solution, 310. $C_{15}H_{15}SAs$ requires C, 59·6; H, 5·0; S, 10·6%; *M*, 304).

Methyldichloroarsine.—We are indebted to Dr. A. F. Crowther for the following modification of Uhlinger and Cook's preparation (*J. Ind. Eng. Chem.*, 1919, **11**, 105). Sodium hydroxide (128 g., 7·6 mols.) and arsenious oxide (84 g., 1 mol.) were dissolved in turn in water (375 c.c.), and the solution stirred mechanically and cooled externally in ice-water whilst methyl sulphate (128 g., 97 c.c., 2·4 mols.) was slowly added. When addition was complete, the solution was heated at 85° for 2·5 hours with continuous stirring. It was then cooled (ice-water), saturated with sulphur dioxide, and dilute sulphuric acid (200 c.c., 1 vol. acid : 9 vols. water) added to decompose the sodium sulphite. The mixture was heated on a boiling water-bath under reflux whilst being saturated with hydrogen chloride; an oil and some solid matter separated. The total product was "steam distilled" in the vapour of constant-boiling hydrochloric acid. The heavy layer of methyldichloroarsine which separated in the distillate was collected, dried (sodium sulphate), and distilled; yield 51 g. (38% of the theoretical), b. p. 133—135°.

2-Methyl-1 : 2 : 3 : 4-tetrahydroisoarsinoline (I; R = Me).—This was prepared as for the phenyl analogue, but by using methyldichloroarsine (29 g., 1 mol.) in place of the phenyl compound. The lower b. p. of the final product allowed distillation at water-pump pressure. The *methylisoarsinoline* was obtained as a liquid, b. p. 130°/16 mm. (6 g., 16% of theoretical), which on refractionation had b. p. 131°/18 mm. (Found: C, 57·4; H, 6·4. $C_{10}H_{13}As$ requires C, 57·7; H, 6·3%). This *iso*arsinoline, when dissolved in excess of cold methyl iodide, readily deposited white crystals. The excess of iodide was allowed to evaporate, and the solid residue recrystallised from alcohol; the *methiodide* was obtained in colourless crystals, m. p. 179—181° [Found: C, 37·9; H, 4·7; ionic I 36·3; I (Carius), 36·5. $C_{11}H_{16}IAs$ requires C, 37·7; H, 4·6; I, 36·3%. The ionic iodine was estimated precisely as above]. This methiodide, in alcoholic solution, treated with picric acid, readily gave the *methopicrate*, m. p. 163—164° after crystallisation from alcohol (Found: C, 45·5; H, 4·35; N, 9·7. $C_{17}H_{18}O_7N_3As$ requires C, 45·2; H, 4·0; N, 9·3%).

Oxidation of (I; R = Me).—(a) *With nitric acid.* Conditions precisely similar to those used for (I; R = Ph) afforded a clear aqueous solution and no crystalline oxide or nitrate could be isolated. The solution was neutralised with sodium hydroxide and on treatment with picric acid solution deposited the *hydroxy-picrate*, which after crystallisation from alcohol had m. p. 164—165·5°, with softening at 160° (Found: C, 42·6; H, 3·7; N, 9·3. $C_{16}H_{16}O_8N_3As$ requires C, 42·4; H, 3·6; N, 9·3%).

(b) *With chloramine-T.* Anhydrous chloramine-T (0·45 g.) was added to a solution of the *iso*arsinoline (0·41 g., 1 mol.) in absolute alcohol (20 c.c.), and the mixture refluxed for 5 mins. The solution, filtered from sodium chloride, was evaporated in a vacuum at room temperature, but the semi-solid, sticky residue could not be crystallised. When treated with cold water, it immediately deposited toluene-*p*-sulphonamide, m. p. and mixed m. p. 136—137°; a portion of the filtrate, treated with picric acid, gave the above hydroxy-picrate; the remainder was concentrated in a vacuum and after removal of a further crop of sulphonamide gave ultimately an oil, which, although presumably the arsine oxide or dihydroxide, could not be obtained crystalline.

A chloroform solution of the *iso*arsinoline (I; R = Me), treated with bromine (1 mol.), rapidly became again colourless. Saturation with hydrogen sulphide, followed by filtration and evaporation of the solvent, gave a viscous oil which slowly solidified to a glass; this was presumably the arsine sulphide, but it could not be crystallised.

2-*Methyl*-1 : 2 : 3 : 4-*tetrahydroisoarsinoline Dichloride.*—A standard solution of chlorine (1 mol.) in carbon tetrachloride was slowly added to the *iso*arsinoline (I; R = Me) in the same solvent at 0°; a white precipitate of the *dichloride* rapidly separated, and, after removal of the solvent in a vacuum, was collected, washed with petrol, and dried (Found: Cl, 23·65. $C_{10}H_{13}Cl_2As$ requires Cl, 25·45%). A portion of this dichloride, dissolved in water and treated with picric acid, gave the above hydroxy-picrate, m. p. and mixed m. p. 165—166°. The remainder was gently heated at 15 mm. pressure; fusion occurred at *ca.* 120°, followed by vigorous effervescence, the pressure rising to 35 mm. The temperature was maintained at 130—140° until decomposition was complete and the pressure again 15 mm.; fractional distillation of the liquid residue then gave 2-*chloro*-1 : 2 : 3 : 4-*tetrahydroisoarsinoline* (I; R = Cl) as a colourless liquid, b. p. 157°/14 mm. (Found: C, 47·6; H, 4·6; Cl, 15·2. $C_9H_{10}ClAs$ requires C, 47·3; H, 4·4; Cl, 15·5%). When a solution of this compound in excess of dry pyridine was boiled for several hours and then fractionally distilled, much of it was recovered unchanged. When the pyridine solution after prolonged boiling was poured into water, a small quantity of solid was obtained; this appeared to be the arsonic acid, formed by hydrolysis and oxidation after the boiling with pyridine. These results, and scarcity of material, caused abandonment of further attempts to prepare 3 : 4-dihydro*iso*arsinoline.

2-*Phenyl*-1 : 2 : 3 : 4-*tetrahydroisophosphinoline Methiodide* (V).—Of the many attempts to prepare the parent *iso*phosphinoline, only the following gave any positive result. A mixture of *o*-β-bromoethylbenzyl bromide (50 g.), phenyldichlorophosphine (32 g., 1 mol.), ether (750 c.c.), sodium wire (40 g., 9·7 atoms), and ethyl acetate (5 c.c.) was refluxed in a nitrogen atmosphere for 12 hours, a further quantity of ethyl acetate (5 c.c.) being added after the first 6 hours. The product was then worked up precisely as described for (I; R = Ph). Final distillation of the residue after removal of the solvent first gave two very small fractions, b. p. 52°/14 mm. and 102°/14 mm.; further distillation of the residue at lower pressure gave a small indefinite fraction, b. p. 130—160°/0·2 mm. This on further refractionation gave a minute fraction which was apparently the crude 2-*phenyl*-1 : 2 : 3 : 4-*tetrahydroisophosphinoline* (Found: C, 83·8; H, 8·0. $C_{15}H_{15}P$ requires C, 79·7; H, 6·6%). The fraction of b. p. 130—160°/0·2 mm. did, however, react vigorously with methyl iodide, and the oily product was ultimately crystallised from alcohol–ether; the pure *methiodide* (V) was thus obtained in colourless crystals, m. p. 116—118° (Found: C, 51·9; H, 4·8. $C_{16}H_{18}IP$ requires C, 52·2; H, 4·9%).

We are greatly indebted to Drs. Brownlee, Bishop, Baldwin, and Friedmann for the therapeutic tests which they have kindly conducted.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 24th*, 1943.]

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146. *The Synthetic Application of* o-β-*Bromoethylbenzyl Bromide. Part III. The Preparation and Optical Resolution of* 2-*Phenyl*-2-p-*chlorophenacyl*-1 : 2 : 3 : 4-*tetrahydroisoarsinolinium Bromide.*

By FREDERICK G. HOLLIMAN and FREDERICK G. MANN.

2-Phenyl-1 : 2 : 3 : 4-tetrahydro*iso*arsinoline readily combines with *p*-chlorophenacyl bromide to give the above *iso*arsinolinium bromide, a salt of considerable stability, which has been resolved into optically active forms *via* the bromocamphorsulphonate. The corresponding *d*- and *l*-*iso*arsinolinium picrates have thus been obtained having $[M]_D$ + 457° and − 450°, and the corresponding *l*-iodide having $[M]_D$ − 354°; both salts are optically stable in chloroform solution at room temperature. These are the first arsonium salts to be obtained in optically stable forms, and the correlation of their optical and chemical stability provides strong evidence that the optical instability previously recorded for dissymmetric arsonium salts has been due to the formation of a " dissociation-equilibrium " in solution. The properties of other dissymmetric 4-covalent arsenic compounds are discussed on this basis.

THE resolution into optically active forms of phenylbenzylmethylallylammonium iodide by Pope and Peachey (J., 1899, **75**, 1127), and the subsequent resolution of several other quaternary ammonium salts of this type, leave little doubt that similar quaternary phosphonium and arsonium salts should also be susceptible to optical resolution, for it is exceedingly unlikely on theoretical grounds that the phosphorus and arsenic compounds possess a configuration essentially different from that of similar nitrogen derivatives.

Nevertheless, it is a striking fact that no phosphorus compound of type [abcdP]X, where a, b, c, d, represent alkyl or aryl groups and X a univalent acid radical, has yet been resolved. Furthermore, although several attempts have been made to resolve a similar arsenic compound [abcdAs]X, only two have been successful, and in both these cases, the arsenic salt possessed only a very small and fleeting optical rotation. For instance, Michaelis (*Annalen*, 1902, **321**, 159) failed to resolve phenyl-*p*-tolylmethylethylarsonium iodide, and Winmill (J., 1912, **101**, 720) also failed with phenylbenzylmethylallylarsonium iodide and other similar salts. Burrows

and Turner (J., 1921, **119**, 426) prepared phenyl-α-naphthylbenzylmethylarsonium bromide, converted it into the *d*-bromocamphorsulphonate, and separated the latter by recrystallisation into two fractions having $[M]_D$ + 281° and + 300° severally. The latter fraction was then converted into the arsonium iodide, which however possessed a fleeting rotation, the highest value measured being $[M]_D$ + 12°. Kamai (*Ber.*, 1933, **66**, 1779; *J. Gen. Chem. Russia*, 1934, **4**, 184) prepared *p*-tolylbenzylethyl-*n*-propylarsonium iodide, converted it into the *d*-bromocamphorsulphonate, and separated the latter similarly into three fractions having $[M]_D$ + 318°, + 291°, and + 285°. The first was converted into an (unanalysed) iodide having $[M]_D$ + 45°, which rapidly racemised in solution; the other two fractions gave inactive iodides. Recently, this author (*ibid.*, 1942, **12**, 104) recorded his failure to obtain any evidence of resolution by the recrystallisation of *p*-tolyl-α-naphthylbenzylethylarsonium *d*-bromocamphorsulphonate and of its β-naphthyl isomer.

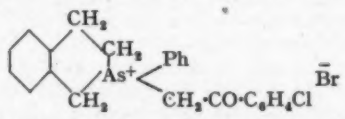
The probable cause of this striking difference in the ease of resolution of dissymmetric quaternary salts of nitrogen compared with those of phosphorus and arsenic is not difficult to formulate. It is known that the optically active quaternary ammonium sulphates and nitrates possess considerable optical stability and are difficult to racemise; the corresponding halides, particularly the iodides, however, racemise much more readily. This racemisation of the iodides is largely determined by the solvent employed: in aqueous solution, the racemisation is slow, but in chloroform solution, even at room temperature, it is comparatively rapid. It was first suggested by Pope and Harvey (J., 1901, **79**, 831) that the racemisation of *d*-phenylbenzylmethylallylammonium iodide in cold chloroform solution was due to the establishment of an equilibrium between the salt and its dissociation products:

$$[N(C_7H_7)(C_6H_5)(C_3H_5)(CH_3)]I \rightleftarrows N(C_6H_5)(C_3H_5)(CH_3) + C_7H_7I$$

This possibility was investigated in detail by other workers (see in particular Wedekind and co-workers, *Ber.*, 1902, **35**, 760; *Z. Elektrochem.*, 1906, **12**, 330; *Ber.*, 1908, **41**, 1029, 2659; von Halban, *Z. Elektrochem.*, 1907, **13**, 57; *Ber.*, 1908, **41**, 2417), and the existence of this dissociation equilibrium conclusively proved. This explains the optical stability of the quaternary ammonium sulphates and nitrates, which of course could not readily undergo a similar dissociation. Burrows and Turner (*loc. cit.*) obtained strong evidence that quaternary arsonium iodides also give rise to a dissociation equilibrium, [abcdAs]I ⇄ abcAs + dI, and attributed the difficulty of obtaining optically stable halide salts to the ready formation of this equilibrium. [It is noteworthy that most dissymmetric quaternary ammonium, phosphonium, and arsonium salts whose resolution has been attempted have for synthetic reasons contained a benzyl radical, which of course lends itself particularly readily to the above dissociation, with formation of benzyl iodide (cf. Snyder and Speck, *J. Amer. Chem. Soc.*, 1939, **61**, 669, 2895).]

Some indirect evidence in favour of this dissociation theory of optical instability as applied to arsonium salts was obtained by Chatt and Mann (J., 1939, 610), who separated ethylene-αβ-bis(phenylmethyl-*n*-butylarsonium picrate) (I) by fractional crystallisation into two isomeric forms, one of which must have been the *meso* and the other the racemic form. The isomerides underwent no interconversion even in boiling alcoholic

(I.) $CH_2{-}\overset{+}{A}sPhMeBu$ | $CH_2{-}\overset{+}{A}sPhMeBu$ $\{O{\cdot}C_6H_2(NO_2)_3\}_2^-$

(II.) 

solution. Such an interconversion, had it occurred, would clearly have involved a change of configuration of one of the asymmetric arsenic atoms in the molecule; this in turn, on the dissociation theory, would have involved formation of a di-tertiary arsine and of an alkyl picryl ether, which is clearly exceedingly unlikely to occur.

The validity of the dissociation theory of the optical instability of arsonium salts could be tested by the attempted resolution of a salt [abcdAs]X, in which a, b, c, d were different *aryl* radicals, and in which dissociation could hardly occur. The preparation of such a salt is possible by Chatt and Mann's aluminium chloride reaction (J., 1940, 1192; 1942, 666) and experiments on these lines will be undertaken when circumstances permit. Meanwhile, we have prepared a suitable salt of another type by combining 2-phenyl-1 : 2 : 3 : 4-tetrahydro*iso*arsinoline with *p*-chlorophenacyl bromide to give the highly crystalline 2-*phenyl*-2-p-*chlorophenacyl*-1 : 2 : 3 : 4-*tetrahydroisoarsinolinium bromide* (II), a salt containing an asymmetric arsenic atom. Now the 1 : 2 : 3 : 4-tetrahydro*iso*arsinoline system is known to possess considerable stability (see previous paper); furthermore, many *p*-chlorophenacyl compounds also have marked stability, far greater than that of the corresponding unsubstituted phenacyl compounds * (cf. Crowther and Mann, this vol., p. 58). Hence it was expected that the quaternary arsonium bromide (II) would possess very considerable stability and undergo no dissociation (other than ionisation) in solution, and thus be capable of resolution into optically stable forms.

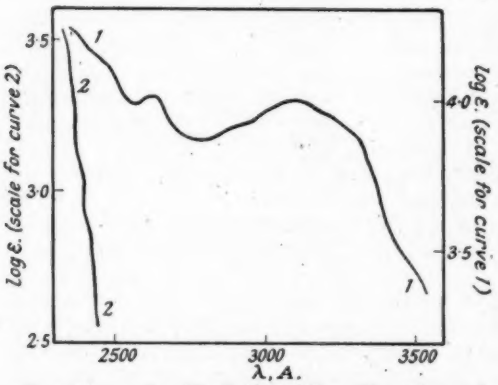
Experiment has fully confirmed our reasoning. The bromide (II) was converted into the d-*bromocamphorsulphonate*, which after recrystallisation from ethyl acetate had m. p. 119—131°, $[M]_D$ + 279° (in chloroform). When, however, this product was extracted with boiling benzene–*cyclo*hexane, the *d-iso*arsinolinium *d*-bromo-

* This difference in stability is well exemplified in the bromides. The pure colourless crystals of phenacyl bromide slowly decompose to a reddish-brown syrup at room temperature even in a dry atmosphere, whereas *p*-chlorophenacyl bromide remains unchanged indefinitely as colourless needles of sharp m. p. under these conditions.

camphorsulphonate dissolved, leaving an insoluble residue of the *l-iso*arsinolinium *d*-bromo-sulphonate, which was readily obtained optically pure by repeated crystallisation from alcohol, and then had m. p. 236—238°, $[M]_D$ — 140°. This salt was converted into l-iso*arsinolinium picrate*, which had $[M]_D$ — 450° (in chloroform), no change in rotation being detected during 24 hours. An acetone solution of this picrate, when treated at 0° with a similar solution of potassium iodide in excess, furnished the crystalline l-iso*arsinolinium iodide*; slight racemisation accompanied this conversion, however, because the iodide so obtained had initially $[M]_D$ — 326°, but recrystallisation from alcohol gave the optically pure iodide having m. p. 176°, $[M]_D$ — 354°, neither constant being changed by further recrystallisation. (For rotations at other wave-lengths, see p. 554.) It is noteworthy that the *dl*-iodide had m. p. 190·5°.

The crude *d-iso*arsinolinium *d*-bromocamphorsulphonate, which had dissolved in the hot benzene–*cyclo*hexane, when isolated had $[M]_D$ + 575° in chloroform and gave the *d-iso*arsinolinium picrate, $[M]_D$ + 354°. Neither of these compounds was optically pure, but their isolation confirms the separation of the two forms from the original *dl-iso*arsinolinium *d*-sulphonate. The optically pure *d-iso*arsinolinium salts were obtained by converting the original racemic bromide (II) into the *l*-bromocamphorsulphonate. Extraction with benzene–*cyclo*hexane now left the insoluble d-iso*arsinolinium* l-*bromocamphorsulphonate*, which after recrystallisation from alcohol had m. p. 236—237°, $[M]_D$ + 140°; this in turn, furnished the optically pure stable d-iso*arsinolinium picrate*, $[M]_D$ + 457°.

It is noteworthy that the *l-iso*arsinolinium iodide underwent no perceptible racemisation in chloroform solution at 15° during 5 days if protected from bright light, which caused slight photochemical decomposition, nor did any appreciable racemisation occur in boiling alcohol, since this solvent was used for the final purification. On the other hand, partial racemisation always occurred when the picrate was converted into the iodide in acetone solution: this slight racemisation apparently occurred during the actual conversion, since no further racemisation could be detected in acetone solution at room temperature. It was, however, increased considerably in boiling aqueous acetone, a sample of the *l*-iodide losing 9% of its activity after 30 minutes' refluxing in this solution. It is probable therefore that in the boiling acetone slight dissociation did occur, with the regeneration of the original tertiary arsine and *p*-chlorophenacyl iodide.



Absorption of: (1) 2-*phenyl*-2-p-*chlorophenacyl*-1 : 2 : 3 : 4-*tetrahydroiso**arsinolinium bromide*; (2) *tetraethylarsonium iodide.*

The reduced arsenical ring in the tetrahydro*iso*arsinolinium ion is undoubtedly "buckled," and this buckling, if rigid, would cause molecular dissymmetry irrespective of individual asymmetric atoms: all stereochemical experience, however, indicates that such buckling would be extremely labile and could not cause molecular dissymmetry, and the optical activity must therefore be due to the asymmetric arsenic atom.

Dr. C. B. Allsopp has kindly investigated the optical properties of the *iso*arsinolinium iodide, and we are indebted to him for the following report:

"The optical rotations observed in the visible spectrum for 4 dm. of a 0·520% solution of *l*-2-phenyl-2-*p*-chlorophenacyl-1 : 2 : 3 : 4-tetrahydro*iso*arsinolinium iodide (p. 554) can be represented, within the limits of experimental error, by the simple dispersion equation $\alpha = -0{\cdot}3816/(\lambda^2 - 0{\cdot}0597)$ (see table below). The dispersion constant in this equation suggests that the optical activity originates mainly in electronic transitions which correspond to absorption at about 2443 A., but it would be necessary to carry the observations to shorter wave-lengths before this point could be decided with certainty.

λ, A.	α, obs.	α, calc.	α, obs. — α, calc.	λ, A.	α, obs.	α, calc.	α, obs. — α, calc.
6708	−1·01°	−0·98°	−0·03°	5461	−1·60°	−1·60°	(±)
6104	−1·20	−1·22	+0·02	5086	−1·93	−1·92	−0·01°
5780	−1·40	−1·39	−0·01	4358	−2·93	−2·93	(±)

"The absorption spectrum of racemic 2-phenyl-2-*p*-chlorophenacyl-1 : 2 : 3 : 4-tetrahydro*iso*arsinolinium bromide, as measured with a Hilger 'Spekker' photometer and intermediate quartz spectrograph, is drawn in the figure. It shows an intense band with a maximum, log ε = 4·01, at 3115 A., and more intense absorption at shorter wave-lengths, log ε>4·24 at 2300 A., with a subsidiary maximum, log ε = 4·02, at 2635 A. The spectrum of the iodide is closely similar, but the chromophore absorbing at 3115 A. (presumably the $\cdot CH_2 \cdot CO \cdot C_6H_4Cl$ radical) is photo-sensitive and began to decompose during the measurements, the solution becoming yellow and detail in the spectrum becoming obscured. All the absorption at wave-lengths above 2500 A. may be attributed to the isolated and substituted phenyl residues, but at least part of that at shorter wave-lengths is due to the arsenic atom, since tetraethylarsonium iodide (Curve 2) gives rise to no absorption except at short wave-lengths, when it is about five times weaker. [At 2550 A., the intensity due to this compound is 300 times less (log ε = 1·45) than that due to the aromatic compounds.]

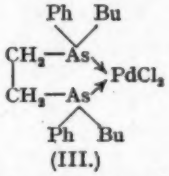
"The calculated anisotropic absorption frequency for the optically active compound lies within this absorp-

tion band, so it is possible that the optical anisotropy of *l*-2-phenyl-2-*p*-chlorophenacyl-1 : 2 : 3 : 4-tetrahydro-*iso*arsinolinium iodide is centred in an electron of the asymmetric arsenic atom. In this it would differ from that of optically active carbon compounds in which the anisotropy is often found to be largely confined to a weakly absorbing chromophoric substituent."

In contrast to the ready resolution afforded by the *iso*arsinolinium bromocamphorsulphonates, it is noteworthy that no evidence of resolution could be obtained in earlier experiments by the recrystallisation of the corresponding *d*-camphorsulphonate.

The optical stability of our *l-iso*arsinolinium iodide in chloroform solution, taken in conjunction with the chemical stability of the *iso*arsinolinium salts, thus affords strong evidence in favour of the dissociation theory of optical instability of quaternary arsonium halides.

The fundamental factor determining the optical stability of other types of 4-covalent arsenic derivatives is, however, not so clear. Chatt and Mann (J., 1939, 1622) separated ethylene-αβ-bis(phenyl-*n*-butylarsine)-dichloropalladium (III) into two isomeric forms, one of which must have been the *meso* and the other the racemic compound; the two forms possessed great stability, and no interconversion occurred either in the molten condition or on prolonged boiling in alcoholic solution. This marked stability is to be expected in



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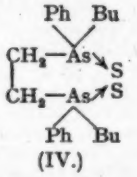

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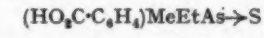


(V.)

this compound, because the co-ordinated ring, for dimensional and structural reasons, is itself very stable, and no dissociation therefore apparently occurs. The corresponding ethylene-αβ-bis(phenyl-*n*-butylarsine sulphide) (IV) was also separated into two similar forms (Chatt and Mann, J., 1939, 610), but in this case the low-melting form very readily passed over into the high-melting form, a conversion which must have entailed a change of configuration of one of the asymmetric arsenic atoms. This result is in marked contrast to those of Mills and Raper (J., 1925, **127**, 2479), who resolved methylethyl-*p*-carboxyphenylarsine sulphide (V) into optically active forms having considerable stability, and no racemisation of these compounds has been recorded. It is possible that in these 4-covalent arsine sulphides, racemisation is similarly dependent on partial dissociation into tertiary arsine and sulphur, and will therefore be dependent in turn on the chemical stability of the particular compound investigated.

If this is true, the ready conversion of the low-melting form of the diarsine disulphide (IV) into the high-melting form is not unexpected. It is well known that if two or more tertiary nitrogen, phosphorus, or arsenic atoms occupy neighbouring positions in a molecule, it is often very difficult to make all these atoms exert simultaneously a covalency of four. This is true, *e.g.*, of the two arsenic atoms in both forms of 5 : 10-di-*p*-tolyl-5 : 10-dihydroarsanthren (Chatt and Mann, J., 1940, 1184) and of the four nitrogen atoms in tetrakis-dimethylaminomethylmethane (Gibson and Mann, J., 1942, 175): many similar instances could be quoted. The explanation of this comparative inertness is doubtless that when, for example, the first arsenic atom in the arsanthren forms a methiodide, the positive charge on this atom exerts a very strong inductive effect, which in turn reduces considerably the normal reactivity of the lone pair of electrons on the second arsenic atom, which consequently becomes inert. The charge on each arsenic atom in the diarsine disulphide (IV) is, however, much weaker than that on a quaternary arsonium atom, and hence does not prevent both atoms showing simultaneously this form of 4-covalency. Nevertheless, the effect must be present, and will facilitate the dissociation, diarsine disulphide $\rightleftarrows$ diarsine monosulphide + sulphur. Even if this equilibrium dissociation should occur only to a minute extent, it will explain the conversion of the less stable form of the disulphide into the more stable.

Experimental.

All rotations were measured in a 4-dm. tube at 16° with (unless otherwise stated) chloroform as solvent, and the sodium-*D* line, λ 5893, as the source of light.

dl-2-*Phenyl*-2-p-*chlorophenacyl*-1 : 2 : 3 : 4-*tetrahydroisoarsinolinium Bromide* (II).—A benzene solution of 2-phenyl-1 : 2 : 3 : 4-tetrahydro*iso*arsinoline (1 mol.) and *p*-chlorophenacyl bromide (1 mol.) was refluxed for 30 mins., separation of the crystalline salt gradually occurring. The mixture was cooled, and the *bromide* (II) collected, washed with benzene, and recrystallised from alcohol; m. p. 190—191° (Found: C, 54·2; H, 4·2. $C_{23}H_{21}OClBrAs$ requires C, 54·8; H, 4·2%). Yield, 80—90% of the theoretical.

The corresponding dl-*iodide* was prepared by the following indirect method. A cold chloroform solution of the bromide was repeatedly shaken with a saturated aqueous solution of sodium picrate. During the fourth extraction, the *iso*arsinolinium picrate separated as a yellow solid, and was collected and washed with water. Evaporation of the chloroform gave a further quantity. An acetone solution of this picrate was then treated with excess of potassium iodide dissolved in acetone containing a few drops of water. The iodide (as II) slowly crystallised, and was then collected, washed with acetone until colourless, and recrystallised from alcohol; m. p. 190·5° (Found: C, 50·2; H, 3·6. $C_{23}H_{21}OClIAs$ requires C, 50·1; H, 3·8%).

The d-*bromocamphorsulphonate* was prepared by gently boiling a solution of the bromide (1 mol.) and silver *d*-bromocamphorsulphonate (1 mol.) in 80% alcohol for 10 minutes, and then evaporating the filtered solution to dryness. The glassy residue was very soluble in methyl and ethyl alcohol, acetone, chloroform, and ethyl acetate; a portion, when dissolved in ethyl acetate and set aside, slowly deposited the crystalline salt. The remainder of the glass was boiled with *cyclo*hexane, and benzene cautiously added until a clear solution was obtained; this solution, when slowly cooled

and seeded with the above crystals, deposited the *d*-bromocamphorsulphonate as white crystals, m. p. 119—131° after softening at 115° (Found : C, 54·4; H, 5·0. $C_{33}H_{35}O_5ClBrSAs$ requires C, 54·0; H, 4·8%). A 1·015% solution had $\alpha + 1{\cdot}54°$, $[M] + 279°$.

Further recrystallisation from benzene–*cyclo*hexane was attempted, but complete solution could not be obtained. The insoluble residue, after thorough extraction with the boiling mixed solvent, was collected and recrystallised from alcohol, the optically pure l-iso*arsinolinium* d-*bromocamphorsulphonate* being readily obtained. The final product of the following crystallisations had m. p. 236—238° with slight previous softening (Found : C, 53·9; H, 4·8%) :

	Concn. of solution, %.	α.	[α].	[*M*].
Once recrystallised	1·198	−0·81°	−17°	−120°
Three times recrystallised	1·270	−0·95	−19	−140
Four times recrystallised	1·160	−0·87	−19	−140

A cold chloroform solution of this pure *l-iso*arsinolinium *d*-sulphonate was shaken with a saturated aqueous solution of sodium picrate for 30 mins.; the chloroform layer, which had become yellow, was separated, and the treatment repeated six times. The chloroform solution of the l-iso*arsinolinium picrate* was then twice washed with water, dried, and evaporated at room temperature; the picrate remained as a friable glass (Found : N, 6·3. $C_{39}H_{33}O_8N_3ClAs$ requires N, 6·45%). A 0·551% solution in chloroform had $\alpha - 1{\cdot}52°$, $[M] - 450°$, and a 0·549% solution in acetone $\alpha - 1{\cdot}135°$, $[M] - 337°$; these rotations were unchanged after the solutions had remained at room temperature for 24 hours.

The l-iso*arsinolinium iodide*. Solutions of the above picrate (2·3 g.) in acetone (80 c.c.) and of potassium iodide (1 g.) in acetone (60 c.c.) containing water (2 c.c.) were mixed at 0° and stirred during 15 mins. The *iodide* (1·7 g.) which had slowly crystallised was then collected and washed with acetone until colourless; m. p. 178·5—179° with darkening from 170° (Found : C, 50·4; H, 4·0; Cl, 6·4; I, 22·8. $C_{33}H_{31}OClIAs$ requires C, 50·1; H, 3·8; Cl, 6·45; I, 23·1%. The Cl and I were calculated from a total halogen estimation, on the assumption that they were present in equiatomic proportion). A 0·519% solution had $\alpha - 1{\cdot}23°$, $[M] - 326°$.

Another preparation of the iodide was carried out precisely as above, for confirmation (Found : C, 49·9; H, 4·1%). A 0·547% solution had $\alpha - 1{\cdot}37°$, $[M] - 345°$. The rotation was unchanged after this solution had been kept in the dark at room temperature for 5 days. On exposure to daylight, however, slight decomposition occurred and the solution became yellow; after 15 hours' exposure, the rotation had fallen to $\alpha - 1{\cdot}22°$, $[M] - 307°$.

The iodide was then crystallised from alcohol until it was optically pure; after one recrystallisation, a 0·517% solution had $\alpha - 1{\cdot}33°$, $[M] - 345°$, and after two recrystallisations, a 0·508% solution had $\alpha - 1{\cdot}30°$, $[M] - 352°$. This pure *l*-iodide had m. p. 176° (Found : C, 50·5; H, 3·8; ionic I, 23·3%. The ionic iodine was estimated volumetrically as described for the phenylmethyl analogue; see previous paper, p. 549).

A 0·520% solution of this iodide gave the following rotations :

Source of light.	A.	α.	[*M*].	Source of light.	A.	α.	[*M*].	Source of light.	A.	α.	[*M*].
Li	6708	−1·01°	−267°	Hg	5780	−1·40°	−370°	Cd	5086	−1·93°	−511°
Li	6104	−1·20	−318	Hg	5461	−1·60	−423	Hg	4358	−2·93	−776

A solution of this pure *l*-iodide (0·5 g.) in a mixture of acetone (32·5 c.c.) and water (1·5 c.c.) was refluxed for 10 mins., the colourless crystals at first forming a white opaque mat but later giving a clear solution. The latter on cooling deposited the iodide (0·45 g.) chemically unchanged, but partly racemised (Found : C, 50·3; H, 4·1%). A 0·416% solution had $\alpha - 0{\cdot}97°$, $[M] - 320°$.

To obtain the *d-iso*arsinolinium ion, the benzene–*cyclo*hexane which had been used to extract the original bromocamphorsulphonate was evaporated to dryness, and the glassy residue extracted with a very small volume of cold alcohol. A small residue was filtered off, and the solution evaporated again to dryness; the glassy product consisted of the optically impure *d-iso*arsinolinium *d*-bromocamphorsulphonate : a 1·095% solution had $\alpha + 3{\cdot}43°$, $[M] + 575°$. This was converted, as already described, into the optically impure *d*-picrate, a 0·553% solution of which had $\alpha + 1{\cdot}20°$, $[M] + 354°$.

The optically pure *d-iso*arsinolinium compounds were obtained by repeating the original resolution, using silver *l*-bromocamphorsulphonate. Extraction of the *iso*arsinolinium *l*-sulphonate with benzene–*cyclo*hexane, followed by repeated alcoholic recrystallisation of the insoluble residue, gave the pure d-iso*arsinolinium* l-*bromocamphorsulphonate*, colourless needles, m. p. 236—237° (Found : C, 54·1; H, 4·8%); a 1·193% solution had $\alpha + 0{\cdot}89°$, $[M] + 140°$. This compound, treated as before, gave the pure d-iso*arsinolinium picrate* (Found : N, 6·1%); a 0·570% solution had $\alpha + 1{\cdot}60°$, $[M] + 457°$.

2-*Phenyl*-2-p-*chlorophenacyl*-1 : 2 : 3 : 4-*tetrahydro*iso*arsinolinium* d-*Camphorsulphonate*.—This was prepared in hot aqueous-alcoholic solution precisely as for the bromocamphorsulphonate. The clear filtrate, when evaporated to dryness, gave at once the crystalline d-*camphorsulphonate*; this was very soluble in methyl and ethyl alcohol, but almost insoluble in ethyl acetate and acetone. It was therefore recrystallised from ethyl alcohol containing 66% of water, from which it tended to separate as an oil which rapidly crystallised on scratching; m. p. 210—212° (Found : C, 59·7; H, 5·5. $C_{33}H_{36}O_5ClSAs$ requires C, 60·5; H, 5·5%). It was repeatedly recrystallised from the aqueous alcohol, without change in m. p.; the fractions obtained (*a*) from the 6th, (*b*) from the 7th recrystallisation, and (*c*) from evaporation of the mother-liquors from the 3rd recrystallisation, gave the following rotations, in 2·347, 2·427, and 1·802% solutions respectively : $\alpha + 1{\cdot}58°$, $1{\cdot}65°$, $1{\cdot}23°$, $[M] + 110°$, $111°$, $112°$.

To determine if resolution was proceeding, an alcoholic solution of the final fraction was treated with the calculated quantity of chloroplatinic acid. The very pale orange iso*arsinolinium chloroplatinate* was collected, and washed with alcohol, water, and alcohol in turn : m. p. 135—150° (decomp.) (Found : C, 43·4; H, 3·1. $C_{46}H_{42}O_2Cl_6As_2Pt$ requires C, 44·0; H, 3·35%). A 2·327% chloroform solution had $\alpha + 0{\cdot}05°$, $[M] + 7°$. No significance is attached to these minute rotations.

This chloroform solution, when set aside overnight, deposited orange needles, and lost its minute rotation. The needles were insoluble in all the usual solvents, and had m. p. 211—213° with softening at 105° (Found : C, 36·3; H, 3·2%). This curious change was not further investigated.

The final fraction of the *d*-camphorsulphonate was similarly converted into the yellow crystalline *chloroaurate*, m. p. 157—158° (Found : C, 35·9; H, 2·8; Au, 26·55. $C_{33}H_{31}OCl_6AsAu$ requires C, 36·2; H, 2·75; Au, 25·8%). A 2·02% solution in acetone showed no activity.

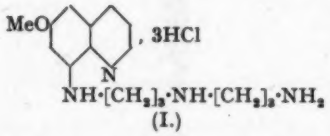
UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 24th*, 1943.]

147. *Attempts to find New Antimalarials. Part XVIII.*

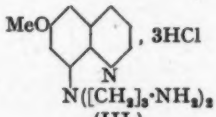
By D. C. Quin and Sir Robert Robinson.

Robinson and Tomlinson (J., 1934, 1524) condensed 8-γ-aminopropylamino-6-methoxyquinoline with phthalo-γ-bromopropylimide and after hydrolysis of the product obtained a hydrochloride (R.63) which proved to be the most potent antimalarial of the plasmoquin series yet encountered. Tested by Professor D. Keilin and his colleagues against *Plasmodium relictum* in canaries, its index was found to be 1/64, which is about twice as good as that of plasmoquin (1/32). These figures are not precise but indicate the order of the activities. The constitution of R.63 is unknown and in the present communication it is shown that two of the more probable structures can be excluded (cf. Part XX).

The most probable structure for R.63 was thought to be (I) and to avoid ambiguity in the synthesis we desired to introduce the side chain *en bloc*. It was found that the phenoxyl group of phthalo-γ-(γ-phenoxypropylamino)propylimide, $PhO{\cdot}[CH_2]_3{\cdot}NH{\cdot}[CH_2]_3{\cdot}N(CO)_2C_6H_4$ (II), could be replaced by bromine and the product was used to attach the complex side-chain to the amino-group of 8-amino-6-methoxyquinoline. On hydrolysis (I) was obtained, but it proved to be almost devoid of antimalarial activity. Similarly, the *hydrochloride* (III), prepared from aminomethoxyquinoline by introducing two γ-phthalimidopropyl groups and subsequent hydrolysis, was found to be a feeble antimalarial. A chlorine atom in position 5 has been found to reduce



(I.)



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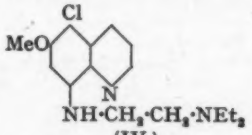
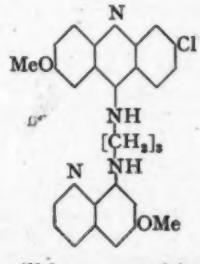


(IV.)

toxicity in the plasmoquin series. The *base* (IV) has been synthesised and is found to have weak antimalarial properties.

The present work was completed in 1937 and included the commencement of an attempt to combine the atebrin and the plasmoquin type. Unfortunately this aspect was not pursued. Condensation of 2 : 5-dichloro-7-methoxyacridine and 8-γ-aminopropylamino-6-methoxyquinoline afforded *2-chloro-5-(6′-methoxyquinolyl-8′-γ-aminopropylamino)-7-methoxyacridine* (V), and dichloromethoxyacridine and 8-γ-phthalimidopropylamino-6-methoxyquinoline gave *2-chloro-5-γ-phthalimidopropylamino-(N-6′-methoxy-8′-quinolyl)-7-methoxyacridine* (VI). It is hoped that an opportunity will be found to repeat these preparations and extend the series.



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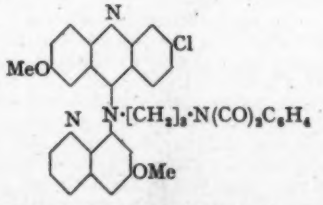

(VI.)

Biological results will be reported in detail by Professor D. Keilin, F.R.S., and his collaborators in another place and this applies also to the following communications. The therapeutic indices mentioned are the ratio of minimum effective dose to maximum tolerated dose for canaries infected with *Plasmodium relictum*.

Experimental.

8-β-Phthalimidoethyl-6-methoxyquinoline.—The condensate from 8-amino-6-methoxyquinoline (30 g., prepared by reducing the nitro-compound with stannous chloride and hydrochloric acid) and phthalo-β-bromoethylimide (48 g.) (Baldwin, J., 1929, 2962) was washed with boiling alcohol (250 c.c.), refluxed with alcohol (100 c.c.), and pyridine added until a homogeneous solution resulted. On cooling, the *base* separated in light yellow prisms (25—30 g.), m. p. 153—155°, and 152° after recrystallisation from acetone (Found: C, 69·6; H, 5·1; N, 12·3. $C_{20}H_{17}O_2N_3$ requires C, 69·1; H, 5·0; N, 12·1%). The hydrochloride has m. p. 248°. After hydrolysis by the hydrazine method, aminoethylamino-methoxyquinoline, b. p. 195—197°/2 mm., is better isolated by means of ether than by means of chloroform, as the latter solvent extracts more impurities.

8-γ-Aminopropylamino-6-methoxyquinoline, prepared according to Baldwin (*loc. cit.*), has b. p. 205°/3 mm., 193°/0·5 mm. Its dihydrochloride has m. p. 252°. 8-γ-Aminopropylamino-6-methoxyquinoline (10·3 g.) was condensed with phthalo-β-bromoethylimide (23·5 g.). After hydrolysis the base was distilled and the fraction, b. p. 223°/0·5 mm., which should contain 8-bis-(β-aminoethyl)-γ-aminopropylamino-6-methoxyquinoline, was tested as hydrochloride (R.81, index 1 : 4—1 : 8). R.80 (index, 1 : 4) and R.89 were hydrochlorides of 8-bis-(γ-aminopropyl)-γ-aminopropylamino-6-methoxyquinoline, b. p. 217°/1 mm., prepared similarly from phthalo-γ-bromopropylimide.

Phthalo-γ-(γ-phenoxypropylamino)propylimide Hydrobromide (as II).—γ-Phenoxypropylamine (Lohmann, *Ber.*, 1891, **24**, 2632) was obtained by hydrazine hydrolysis of the related phthalimide (70% yield, using phenoxypropyl bromide, phthalimide, and potassium carbonate) in about 90% yield. A mixture of the amine (20 g.), phthalo-γ-bromopropylimide (34·5 g.), and dioxan (60 c.c.) was refluxed for 8 hours. The cold solution was filtered from phenoxypropylamine hydrobromide, m. p. 176°, and a second crystallisation could be induced by scratching. This *salt*, twice crystallised from methanol, had m. p. 184° and a mixture with that of m. p. 176° had m. p. 153°. It did not depress the m. p. of

a specimen, previously obtained from a condensation in xylene solution, which had been analysed (Found: C, 57·0; H, 5·6; N, 6·1. $C_{20}H_{22}O_2N_2$,HBr requires C, 57·2; H, 5·5; N, 6·7%).

Phthalo-γ-(γ-bromopropylamino)propylimide Hydrobromide.—A mixture of the above salt (5 g.) and hydrobromic acid (15 c.c., saturated at 0°) was heated in a sealed tube at 100° for 2·5 hours. After addition of water (40 c.c.), phenol was removed by extraction with ether and during this process the *product* crystallised. It separated from methanol in colourless prismatic needles (0·75 g.), m. p. 195° (Found: C, 41·8; H, 4·7; N, 6·4; Br, 38·3. $C_{14}H_{16}O_2N_2$,HBr requires C, 41·4; H, 4·4; N, 6·9; Br, 39·4%).

8-*γ-Phthalimidopropyl-γ-aminopropylamino-6-methoxyquinoline Dihydrobromide.*—A mixture of the last-mentioned salt (2 g.), 8-amino-6-methoxyquinoline (0·8 g.), and dioxan (10 c.c.) was refluxed for 8 hours. After cooling, the residue was collected and crystallised from methanol; m. p. 222—223° (Found: N, 9·9; Br, 27·1; MeO, 4·8. $C_{24}H_{26}O_3N_4$,2HBr requires N, 9·7; Br, 27·6; 1MeO, 5·3%). Hydrolysis by means of hydrazine, followed by conversion into a hydrochloride, afforded crude 8-*γ-aminopropyl-γ-aminopropylamino-6-methoxyquinoline trihydrochloride* (I, R.92) (inactive at the maximum tolerated dose) as an exceedingly deliquescent, yellow powder (Found: N, 14·4; Cl, 24·8; MeO, 7·8. $C_{16}H_{24}ON_4$,3HCl requires N, 14·1; Cl, 26·8; 1MeO, 7·8%). The analysis indicates replacement of a part of the hydrogen chloride by water.

2 : 4-*Dinitro-β-aminoethylaniline.*—Condensation of 1-chloro-2 : 4-dinitrobenzene (10 g.) and ethylenediamine (9 g.) in boiling alcohol (75 c.c.) gave a mixture of the required product and bisdinitrophenylethylenediamine. The latter was separated by taking advantage of its sparing solubility in hot 10% hydrochloric acid. The filtrate deposited the *hydrochloride* (8·5 g.), m.p. 250° (decomp.) (Found: C, 36·9; H, 4·3; N, 21·7. $C_8H_{10}O_4N_4$,HCl requires C, 36·5; H, 4·2; N, 21·4%). The free *base* crystallised from aqueous alcohol in yellow plates, m. p. 54°, identical with a specimen later prepared from 2 : 4-dinitroanisole and ethylenediamine (Found: C, 42·6; H, 4·5; N, 24·7. $C_8H_{10}O_4N_4$ requires C, 42·5; H, 4·4; N, 24·8%).

2 : 4-*Dinitro*-N-*γ-phenoxypropyl-β-aminoethylaniline Hydrochloride.*—A mixture of dinitrophenylethylenediamine (8·5 g.), potassium carbonate (8·5 g.), γ-phenoxypropyl bromide (8 g.), and ethyl acetate (100 c.c.) was refluxed for 5 hours. The solvent was evaporated, and the residue extracted with warm ether. The *hydrochloride* was precipitated from the combined extracts by passage of hydrogen chloride and crystallised from alcohol; yield, 11 g., m. p. 114° (Found: C, 51·7; H, 5·5; N, 14·2; Cl, 8·8. $C_{17}H_{20}O_5N_4$,HCl requires C, 51·5; H, 5·3; N, 14·2; Cl, 9·0%). The next stage was to have been the replacement of the phenoxyl group by bromine, but this was abandoned when it was found possible to use phthalimido instead of dinitrophenyl as a protecting group.

8-*Di-γ-phthalimidopropylamino-6-methoxyquinoline.*—(*a*) A mixture of 8-γ-phthalimidopropylamino-6-methoxyquinoline (5·5 g.) and phthalo-γ-bromopropylimide (4·1 g.) was heated at 120° for 6 hours. The product was treated with boiling alcohol, leaving a residue of phthalimidopropylaminomethoxyquinoline hydrobromide; the solution afforded more of the unchanged materials, which were removed. The filtrates were evaporated; the straw-coloured residue contained a substance which was very sparingly soluble in boiling alcohol, although it had not previously separated (0·07 g. required 1 l. for solution). The fawn-coloured needles (Found: C, 61·8; H, 5·2; N, 8·4; Br, 11·7. $C_{32}H_{28}O_5N_4$,HBr requires C, 61·0; H, 4·6; N, 8·9; Br, 12·8%) were treated with hot aqueous sodium carbonate; the *base* crystallised from alcohol, in which it was very sparingly soluble, in colourless feathery needles (0·5 g.), m. p. 166° (Found: C, 70·2; H, 5·3; N, 10·6; MeO, 4·8. $C_{32}H_{28}O_5N_4$ requires C, 70·0; H, 5·1; N, 10·2; 1MeO, 5·7%). The condensation was also effected in boiling dioxan with the same results.

(*b*) The same substance, identified as the base, was also obtained as a by-product of the condensation of 8-amino-6-methoxyquinoline and phthalo-γ-bromopropylimide at 120—130° under the conditions prescribed by Baldwin (*loc. cit.*). A mixture of the bis-phthalimide (1·5 g.), hydrazine hydrate (0·275 c.c.), and alcohol (50 c.c.) was refluxed for 3 hours, the solvent removed, and the residue heated on the steam-bath for ½ hour, cooled, and filtered through kieselguhr. The basified filtrate was extracted with ether, and the hydrochloride precipitated from the dried solution by passage of hydrogen chloride as a very deliquescent yellow solid. It was dissolved in alcohol and reprecipitated with ether (R.93, index 1 : 2). Five years later the preparation was repeated, and the salt obtained in yellow needles by keeping an alcoholic solution in ether vapour under diminished pressure (Found in material dried in a high vacuum at 110°: C, 48·2; H, 7·0; N, 14·0; Cl, 26·7. $C_{16}H_{23}ON_4$,3HCl requires C, 48·4; H, 6·8; N, 14·1; Cl, 26·8%). It is therefore 8-*bis-γ-aminopropylamino-6-methoxyquinoline trihydrochloride* (III).

5-*Chloro*-8-*β-diethylaminoethylamino-6-methoxyquinoline.*—5-Chloro-8-amino-6-methoxyquinoline has m. p. 154° (Robinson and Tomlinson, *loc. cit.*, give m. p. 150—152°). It was condensed in alcoholic solution with β-chlorotriethylamine hydrochloride following the general method of Magidson and Strukov (*Arch. Pharm.*, 1933, **271**, 359), according to which the mixture is heated on the steam-bath and alcohol allowed slowly to evaporate by way of an inefficient condenser. The basic *product* (2 g. from 3 g.) crystallised from alcohol in light yellow plates, m. p. 76° (Found: C, 62·9; H, 7·5; N, 13·4; Cl, 12·0. $C_{16}H_{22}ON_3Cl$ requires C, 62·5; H, 7·2; N, 13·7; Cl, 11·5%). The dihydrochloride (R.86) crystallised from alcohol in reddish-orange, stellate clusters of needles, m. p. 179—181°.

2-*Chloro*-5-(6′-*methoxyquinolyl*-8′-*γ-aminopropylamino*-7-*methoxyacridine* (V).—A mixture of 2 : 5-dichloro-7-methoxyacridine (2·8 g.), 8-γ-aminopropylamino-6-methoxyquinoline (2·3 g.), and phenol (7·5 g.) was heated on the steam-bath for 10 hours. After washing with ether, the residue was triturated with dilute hydrochloric acid and then with alcohol. The bright yellow hydrochloride was heated at 80° with aqueous sodium acetate, the base collected and dissolved in acetic acid, and the solution poured in a thin stream with stirring into dilute aqueous ammonia. The *substance* (V), crystallised from ether and from benzene, had m. p. 114° (Found: C, 62·7; H, 5·9; N, 10·2; Cl, 6·7; MeO, 12·2. $C_{27}H_{25}O_2N_4Cl$,3H_2O requires C, 62·2; H, 6·0; N, 10·4; Cl, 6·8; 2MeO, 12·2%). The *dihydrochloride* formed yellow needles from alcohol, m. p. 223° (decomp.) (Found: C, 58·9; H, 4·9; N, 10·7; MeO, 11·1. $C_{27}H_{25}O_2N_4Cl$,2HCl requires C, 59·1; H, 5·0; N, 10·1; 2MeO, 11·4%).

The *compound* (VI) was obtained by heating a mixture of 2 : 5-dichloro-7-methoxyacridine (3·8 g.), 8-γ-phthalimidopropylamino-6-methoxyquinoline (5·0 g.), and phenol (12 g.) for 8 hours at 100°. The mass was extracted with ether and then with boiling alcohol (3 × 100 c.c.). The residual red hydrochloride became yellow on treatment with aqueous ammonia. The base was collected and extracted with more hot alcohol (300 c.c.); it crystallised from much boiling alcohol, in which it was very sparingly soluble, in needles which collapsed at *ca.* 140° and then had m. p. 253° (decomp.) (Found: N, 8·6. $C_{35}H_{27}O_4N_4Cl$,3H_2O requires N, 8·5%).

The work was interrupted at this stage, but a hydrolysed hydrochloride was prepared by the usual hydrazine process. It formed bright scarlet crystals which became purplish at 100°. The dark carmine aqueous solution became yellow on dilution, probably as the result of hydrolysis.

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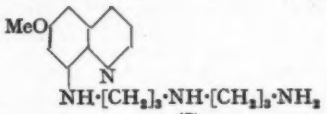
148. *Attempts to find New Antimalarials. Part XIX.*

By W. L. Glen and Sir Robert Robinson.

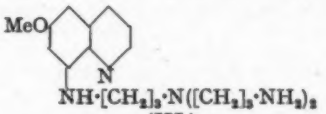
New preparations of R. 63 (see preceding paper) have been made, and the high antimalarial activity confirmed by our biological colleagues. Fractionation of the meconates has afforded no specimen of higher activity and indeed a disconcerting result in some cases has been the reduction of activity in all fractions without traceable loss of material. No light has been shed on the nature of R. 63 by the synthesis of various substances that might have been produced in the formation reaction. A number of new antimalarials of the plasmoquin series have been prepared, including moderately long chains and, in some cases, amidine groups. One of these compounds is a potent antimalarial worthy of more extended biological examination.

R. 63 is obtained by a process which should be the γ-aminopropylation of 8-γ-aminopropylamino-6-methoxyquinoline. We have prepared a *meconate* which gave moderately satisfactory analytical figures for the dimeconate of 8-γ-aminopropyl-γ-aminopropyl-6-methoxyquinoline (I), but independent syntheses of this base (see the preceding and the following paper) have been effected and its salts are devoid of antimalarial properties.



(I)

(II.)



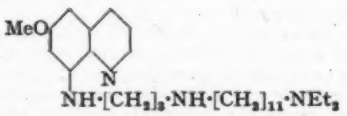
(III.)

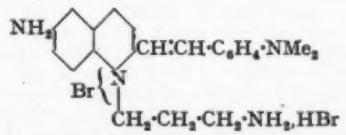
Whereas the indices of the hydrochloride and meconate of the analysed specimen were returned as 1 : 32, we describe a process of fractionation which has twice given a meconate with an index 1 : 64. This was also reported for the original specimen of R. 63 and for a specimen later prepared in the same way by Dr. D. C. Quin. It is certain that the active substance is not (II) or (III) and indeed the use of more than one equivalent of phthalo-γ-bromopropylimide leads to a product with greatly diminished activity.

In view of the consistent nitrogen content of active specimens it appeared improbable that a great departure from the structures (I) and (II) could be contemplated and this led us to study the demethylation of these bases. The results were of a negative character and further work in this direction is planned.

A problem somewhat similar to that of R. 63 is presented by R. 97 which, from its method of preparation, should be the meconate of (IV). The index was reported to be 1 : 62, but unfortunately the salts of the base could not be crystallised. With three methylene groups instead of eleven, the index of a similar crude preparation was 1 : 32. It is hoped that these substances may be prepared in a state of purity by the methods described in the following paper.

(IV.)





(V.)

The introduction of an amidine group into the side chain is described in the experimental section, but the products were weak antimalarials. The *bromide hydrobromide* (V) has been prepared by a series of reactions; it has no antimalarial properties, but is antiseptic and trypanocidal.

Experimental.

8-γ-Phthalimidopropylamino-6-methoxyquinoline.—The prescription of Baldwin (J., 1929, 2962) has been modified as follows: 8-Amino-6-methoxyquinoline (87 g.) and phthalo-γ-bromopropylimide (134 g.) were slowly heated to 100°, and when a homogeneous melt was obtained the temperature was cautiously raised to 110° and maintained for 20 minutes. Heat was generated and the temperature had to be carefully controlled. When the initial reaction had subsided, the mixture was heated (bath at 120°) for 10 hours. On cooling, an orange-yellow mass of mixed hydrobromides was obtained; this was powdered and extracted with a little alcohol to remove unchanged phthalo-γ-bromopropylimide. The salts were extracted with hot water and finally with dilute hydrochloric acid: 20—30% of aminomethoxyquinoline was recovered from the solutions. The insoluble residue was suspended in boiling alcohol, and pyridine slowly added until complete solution occurred (cf. the preceding paper). After 12 hours the product was collected, washed with a little alcohol, dried, and crystallised from alcohol containing a little pyridine; m. p. 100—101° (yield, 80 g.).

The alcohol–pyridine mother-liquor was diluted with a little water and kept for several days. The solid deposit was crystallised from a large volume of alcohol (yield, 10 g.) and obtained in small colourless needles, m. p. 166—167°, and proved to be diphthalimidopropyl-8-amino-6-methoxyquinoline (Found: C, 70·1; H, 5·1; N, 10·3. Calc. for $C_{32}H_{28}O_5N_4$: C, 70·0; H, 5·1; N, 10·3%).

An alcoholic solution of 8-γ-aminopropylamino-6-methoxyquinoline (Baldwin, *loc. cit.*) was treated with an excess of alcoholic meconic acid, and the precipitated *meconate* collected and extracted with boiling alcohol. The salt separated from aqueous alcohol (1 : 1) as an amorphous yellow powder, m. p. 165—166° (decomp.), soluble in hot alcohol, but readily soluble in hot water (Found: C, 50·2; H, 4·3; N, 6·7. $C_{18}H_{17}ON_3,2C_7H_4O_7,H_2O$ requires C, 50·0; H, 4·2; N, 6·5%).

R. 63.—8-γ-Aminopropylamino-6-methoxyquinoline (3 g.) and phthalo-γ-bromopropylimide (3·5 g.) were heated together at 115° for 7 hours. On cooling, a glassy mass was obtained, which was pulverised and obtained as a yellow powder (5·3 g.). The product was insoluble in ether, partly soluble in chloroform and in water, and completely soluble in boiling alcohol; the solutions deposited a sticky, intractable mass on cooling. A portion was basified, and the buff-coloured, sticky base converted into meconate, tartrate, and picrate, but these derivatives could not be crystallised.

A mixture of the crude hydrobromide (10 g.), alcohol (100 c.c.), and hydrazine hydrate (2 g.) was refluxed for 2 hours.

The solvent was removed, and the residue heated with excess of dilute hydrochloric acid for ½ hour on the steam-bath. Phthalhydrazide separated, and an orange-yellow solution was obtained, which was cooled in ice and filtered, and potassium carbonate added to form a pasty mass. This was extracted with chloroform, the extract dried, and hydrogen chloride passed into the filtered solution. The red hydrochloride which separated was washed with chloroform and dried over phosphoric oxide. It was a dark red, extremely deliquescent, amorphous substance which possessed a high antimalarial activity (Keilin) comparable with that of the product of Robinson and Tomlinson.

Exactly similar conditions were used for the condensation of 8-γ-aminopropyl-6-methoxyquinoline (1 mol.) with phthalobromopropylimide (*a*, 0·5; *b*, 1·0; *c*, 1·5 mols.). The crude hydrochlorides were dissolved in hot alcohol with exclusion of moisture. On cooling, a flocculent red precipitate separated, which was collected and washed with alcohol out of contact with the atmosphere. In each case a dark red powder was obtained, and the products were increasingly deliquescent as the proportion of phthalobromopropylimide was increased. The combined washings and mother-liquor from each experiment were evaporated to dryness in case they contained active material. The results of biological tests were as follows: Therapeutic indices, (*a*) 1 : 32, (*b*) 1 : 32, (*c*) 1 : 8 and indices of material recovered from mother-liquors (*a*) 1 : 16, (*b*) 1 : 16, (*c*) 1 : 4. In each case the activity of the material recovered from the mother-liquor was lower than that of the main product, indicating that active material had not been lost in the course of purification. As nothing was gained by variation of the proportions of the reagents, equivalent quantities were employed in all subsequent experiments.

The meconate was prepared from "R. 63" base by treatment with an excess of hot alcoholic meconic acid. The precipitate was collected and washed with hot alcohol. It was an orange-yellow powder which darkened at 140—150°, and swelled and decomposed *ca.* 150—160°. Analysis showed that two molecules of meconic acid had combined with one of the base (Found: C, 49·5; H, 5·2; N, 7·9. $C_{16}H_{24}ON_4,2C_7H_4O_7,2H_2O$ requires C, 49·8; H, 5·0; N, 7·8%). This calculation is based on the assumption that the main product is an aminopropyl derivative of aminopropylaminomethoxyquinoline. On drying over phosphoric oxide in a high vacuum, 0·8322 g. lost 0·0384 g.; $2H_2O$ requires loss, 0·0414 g. (Found in anhydrous material: C, 52·9; H, 4·8; N, 8·5. $C_{16}H_{24}ON_4,2C_7H_4O_7$ requires C, 52·3; H, 4·7; N, 8·1%). The *meconate* was readily soluble in water, but non-deliquescent. The therapeutic index was 1 : 32 and therefore equal to that of the hydrochloride.

The *tartrate* was prepared in hot alcoholic solution, at once collected, washed with alcohol, and dried in a desiccator. It was obtained as a brownish-red amorphous powder, slightly deliquescent, and readily soluble in water (Found: C, 49·0; H, 6·4; N, 9·5. $C_{16}H_{24}ON_4,2C_4H_6O_6$ requires C, 49·0; H, 6·1; N, 9·5%). The index was reported as 1 : 8. The citrate also was prepared, but neither of these salts offered any advantage over the meconate.

8-γ-Aminopropylamino-6-methoxyquinoline (4·6 g.) and phthalo-γ-bromopropylimide (5·5 g.) were condensed as usual, and the R. 63 base solution saturated with potassium carbonate. The solution was extracted with chloroform (100 c.c.), and the base converted into meconate (i) (3·2 g.). Two more extractions (300 c.c.) and conversion into meconate gave (ii) (0·3 g.). (iii) (3·7 g.) was obtained similarly after addition of much solid potassium carbonate and exhaustive extraction. Fractions (i) and (ii) were orange-yellow powders and (iii) was somewhat darker in colour. This experiment was repeated (*b*) and Professor Keilin reports the following indices: (i *a*) and (i *b*), 1 : 64; (ii *a*) and (ii *b*), 1 : 32; (iii *a*), 1 : 4; (iii *b*), 1 : 8. Many similar fractionations have been carried out and always with the result that the highest activity (1 : 64) occurs in the base first extracted. Attempts to separate (i) into its constituents by treatment with solvents gave fractions which were all reported of lower activity than the original. In view of the possibility of the presence of hydrazine meconate in these specimens, the salt was prepared but, as expected, was found to be entirely devoid of antimalarial activity.

Further di-γ-phthalimidopropyl-8-amino-6-methoxyquinoline was hydrolysed by the hydrazine method, and the base converted into a meconate (Found: C, 55·5; H, 4·6; N, 7·4%). It was also bisaminopropylated and converted into meconate. Neither of these salts was a potent antimalarial (indices of both, 1 : 2).

Phthalo-ω-bromodecylimide.—A mixture of decamethylene dibromide (145 g.), powdered potassium carbonate (19 g.), and phthalimide (36 g.) was heated for 6 hours at 160—170°. The mass was cooled and extracted with hot water; on keeping, the oil solidified. Unchanged decamethylene dibromide was removed by extraction with successive quantities of alcohol at 30—40°. The product was extracted with light petroleum (Soxhlet), and *phthalobromodecylimide* (32 g., 35%) separated from the solution and crystallised from alcohol, forming small colourless prisms, m. p. 57—58° (Found: C, 59·8; H, 6·6; N, 3·9. $C_{18}H_{24}O_2NBr$ requires C, 59·0; H, 6·6; N, 3·8%). The residue in the thimble was crystallised from alcohol; m. p. 135—136° (6·5 g.) (Braun, *Ber.*, 1909, **42**, 4541, gives m. p. 136° for diphthalimidodecane); 30 g. of dibromodecane were recovered.

8-ω-*Phthalimidodecylamino*-6-*methoxyquinoline.*—A mixture of phthalo-ω-bromodecylimide (23 g.) and 8-amino-6-methoxyquinoline (13·5 g.) was heated at 100—110° for 24 hours. The orange-yellow crystalline mass was repeatedly extracted with hot water, and the residue triturated with aqueous sodium carbonate solution, washed with water, and extracted with ether. The ethereal extract was shaken with a little concentrated hydrochloric acid, and the resulting yellow precipitate of 8-ω-*phthalimidodecylamino*-6-*methoxyquinoline hydrochloride* collected and washed with ether. After crystallisation from alcohol, it had m. p. 151—153° (decomp.) (Found: C, 68·2; H, 7·0. $C_{28}H_{33}O_3N_3,HCl$ requires C, 67·8; H, 6·9%).

The crude hydrochloride was triturated with warm 10% sodium carbonate solution, and the free *base* obtained as a viscous oil which ultimately solidified on scratching and keeping. The substance was repeatedly crystallised from alcohol, and formed greenish-yellow prisms (9 g.), m. p. 83—84° (Found: C, 73·0; H, 7·1; N, 9·2. $C_{28}H_{33}O_3N_3$ requires C, 73·0; H, 7·2; N, 9·2%).

8-ω-*Aminodecylamino*-6-*methoxyquinoline Dihydrochloride* (R. 95; index, 1 : 7).—A solution of 8-ω-phthalimidodecylamino-6-methoxyquinoline (5·5 g.) and hydrazine hydrate (6·6 c.c.) in alcohol (80 c.c.) was refluxed for 2 hours; a colourless product then separated from the hot solution. The alcohol was evaporated, and the residue heated with an excess of 10% hydrochloric acid for ½ hour on the steam-bath. After standing for 12 hours, the filtrate from phthalhydrazide was basified and extracted with ether. The ethereal solution of the free base was dried, and the *dihydrochloride* precipitated in the usual manner (4 g., 83%). The salt was readily soluble in water, giving a clear orange-yellow solution which became turbid when much diluted, indicating hydrolysis. It crystallised from alcohol in orange-red prisms, m. p. 172° (Found: C, 59·5; H, 8·0; N, 10·1; Cl, 17·2. $C_{20}H_{31}ON_3,2HCl$ requires C, 59·6; H, 8·2; N, 10·4; Cl, 17·6%).

8-ω-*Aminodecyl*-ω-*aminodecylamino*-6-*methoxyquinoline.*—8-ω-Aminodecylamino-6-methoxyquinoline (1·8 g.) was heated with excess of phthalo-ω-bromodecylimide for 24 hours at 100—110°. The product was extracted several times with hot water and once with dilute hydrochloric acid, and the insoluble residue dried. The pulverised product was triturated with ether, then basified, and extracted with chloroform. After evaporation the residue (2·4 g.) was refluxed for 2 hours with hydrazine hydrate (0·3 c.c.) and alcohol (20 c.c.), then evaporated to dryness and heated on the steam-bath for ½ hour with an excess of dilute hydrochloric acid. The orange-red filtrate from phthalylhydrazide was treated with sodium carbonate and extracted with ether. The solvent was removed, and alcoholic meconic acid added. The orange-coloured *meconate* was collected and washed with warm alcohol, followed by ether, and finally dried in a desiccator. The product was readily soluble in water to an orange solution (Found: C, 60·7; H, 6·5; N, 6·8. $C_{30}H_{53}ON_4,2C_7H_4O_7$ requires C, 59·8; H, 6·8; N, 6·4%). The substance is a weak antimalarial.

8-ω-Aminodecyl-γ-aminopropylamino-6-methoxyquinoline.—A mixture of 8-γ-aminopropylamino-6-methoxyquinoline (1·5 g.) and phthalo-ω-bromodecylimide (3·1 g.) was heated for 24 hours at 100—101°. The product was repeatedly extracted with hot water until the extracts were almost colourless, and the process repeated with hot dilute hydrochloric acid. The residue was dried, washed with ether, basified, and extracted with ether. Dry hydrogen chloride was passed into the dried ethereal solution and the oily red hydrochloride obtained was collected, freed from ether, and basified with aqueous sodium carbonate. All attempts to obtain the base in solid form failed, so it was rendered to chloroform and dried, and the solution evaporated. The residual 8-ω-phthalimidodecyl-γ-aminopropylamino-6-methoxyquinoline (1·7 g.) was dissolved in alcohol (10 c.c.) and refluxed with an excess of hydrazine hydrate for 1½ hours; a solid then separated. The alcohol was distilled, and the residue heated with an excess of dilute hydrochloric acid for ½ hour on the steam-bath. The orange solution was filtered, made alkaline, and extracted with ether. The ethereal extract was dried, filtered, and excess of a cold, saturated solution of meconic acid in alcohol added. The *meconate* which separated was collected and washed with alcohol and ether. 0·5 G. of a yellow powder, m. p. 160—164°, was obtained (Found : C, 57·5; H, 6·4; N, 7·9. $C_{23}H_{38}ON_4.2C_7H_4O_7$ requires C, 56·4; H, 5·9; N, 7·1%). We have frequently found that meconates of known bases have anomalous compositions and an analysis such as this indicates the presence of less than the equivalent of meconic acid in the salt.

Condensation of 8-γ-Aminopropylamino-6-methoxyquinoline and 11-Chloro-1-diethylaminoundecane Hydrochloride.—Equivalent quantities of the two reactants were dissolved in a little alcohol and heated for 40 hours at 115—120° in a flask fitted with a short air-condenser. The product was dissolved in a small volume of chloroform, and cold alcoholic meconic acid added until precipitation of the meconate was complete. The product was collected and washed with alcohol, and the filtrate and washings set aside. The meconate was dissolved in a mixture of water (30 c.c.) and alcohol (20 c.c.), and the solution filtered. A yellow powder separated, which was collected, washed with alcohol, and dried. It melted at *ca.* 155°. This material was submitted to biological test (Fraction I) and proved to be a potent antimalarial (R. 97; index, 1 :.62).

The filtrate and washings were evaporated to dryness under reduced pressure, and the residue dissolved in water, basified, and extracted with ether. The ethereal extract was dried, and dry hydrogen chioride passed. The very hygroscopic, red hydrochloride which separated was washed with ether and dried (Fraction II). This material had only moderate antimalarial activity (R. 99; index, 1 : 8). Satisfactory analyses of these salts were not obtained.

Condensaiton of 8-γ-Aminopropylamino-6-methoxyquinoline and 3-Chloro-1-diethylaminopropane Hydrochloride.—8-γ-Aminopropylamino-6-methoxyquinoline (10·5 g.) and 3-chloro-1-diethylaminopropane hydrochloride (8·5 g.) (Magidson and Strukov, *Arch. Pharm.*, 1933, **271**, 572) were heated together at 110—120° for 48 hours. On cooling, an orange-red semi-solid mass was obtained, which was triturated with ether, basified, and extracted with chloroform. The extract was dried, filtered, and evaporated to dryness under reduced pressure. The residue was dissolved in hot alcohol and treated with an excess of meconic acid in the usual manner. The meconate was collected, washed with hot alcohol, and dried in a vacuum desiccator (R. 113). An amorphous yellow powder was obtained which decomposed between 160° and 165°. Attempts to fractionate a chloroform solution of the free base by adsorption on alumina were unsuccessful. R. 113 is a potent, non-toxic, antimalarial (index, 1 : 32).

Condensation of 8-γ-Aminopropylamino-6-methoxyquinoline and 2-Bromo-5-diethylaminopentane Hydrobromide.—Equivalent quantities (7·7 g. and 10 g. respectively) were heated together at 120° for 15 hours. The mixture was cooled, digested with warm dilute hydrochloric acid, basified, and extracted with chloroform. The solvent was removed from the dried extract, and the residue dissolved in alcohol, filtered, and treated with excess of alcoholic meconic acid solution. The meconate was collected, washed with alcohol, and dried; it was a yellow powder, m. p. 150—155° (decomp.) [R. 103; two fractions separated (*a*) from alcohol, (*b*) from water, indices of both, 1 : 32].

8-γ-p-Acetamidobenzenesulphonamidopropylamino-6-methoxyquinoline.—Equivalent quantities of 8-γ-aminopropylamino-6-methoxyquinoline and *p*-acetamidobenzenesulphonyl chloride were heated for 1 hour at 40—50° in dry chloroform solution. After 12 hours, the mixture was diluted with ether, the precipitated material collected and extracted with warm dilute hydrochloric acid, and the solution filtered and cooled. The filtrate was neutralised with dilute aqueous ammonia, and the precipitated base collected, thoroughly washed with water, and dried. Difficulty was experienced in crystallising the product; it was purified by solution in alcohol and reprecipitation with ether, the process being repeated several times. A dark brown *product*, m. p. 189°, was obtained (Found : C, 58·2; H, 6·1; N, 13·0. $C_{31}H_{34}O_4N_4S$ requires C, 58·8; H, 5·6; N, 13·1%).

The meconate, prepared in the usual manner, was readily soluble in water, and formed a yellow powder which darkened at 158° and decomposed between 158° and 168°.

11-Diethylaminoundecanol.—The method of Magidson and his collaborators (*Arch. Pharm.*, 1935, **273**, 320) was modified. A solution of ethyl 11-diethylaminoundecoate (20 c.c.) in ethyl alcohol (200 c.c.) was added very quickly to molten sodium (20 g.) in a flask (bath at 150°) fitted with a very efficient, wide condenser. After 20 minutes alcohol (100 c.c.) was added, followed, after another 20 minutes, by another 100 c.c. The mixture was refluxed for 1 hour.

The products of several such reductions were combined, and the mass cautiously diluted with water and steam-distilled. The residue was cooled, and the oily layer separated, washed thrice with hot water, and rendered to ether. The washings were cooled and extracted with ether, and the combined ethereal solutions dried. The solvent was removed, and the residue fractionated. The yield was 13 g., b. p. 180—184°/20 mm., from 20 c.c. of ester. Conversion into the chloride hydrochloride followed the description of Magidson (*loc. cit.*), but the reaction with thionyl chloride was advantageously effected at − 5°.

5-Chloro-8-ω-diethylaminoundecylamino-6-methoxyquinoline Hydrochloride (R. 98).—A mixture of 5-chloro-8-amino-6-methoxyquinoline (10·5 g.), 11-diethylaminoundecyl chloride hydrochloride (15·0 g.), and alcohol (10 c.c.) was heated for 24 hours at 100—110° and then for 24 hours at 110—120°. A short air condenser was used, so that the alcohol gradually evaporated. The red, crystalline mass was triturated with ether, and the solid matter collected and thoroughly washed with ether. It was then extracted with alcohol, leaving a residue of 5-chloro-8-amino-6-methoxyquinoline hydrochloride (the free base, after crystallisation from methyl alcohol, melted at 149—150° and caused no depression of m. p. when mixed with an authentic specimen of 5-chloro-8-amino-6-methoxyquinoline).

The alcoholic solution was concentrated, cooled, and diluted with a large volume of ether; *5-chloro-8-ω-diethylaminoundecylamino-6-methoxyquinoline hydrochloride* was then precipitated. After crystallising from alcohol and from alcohol–ether, it formed small, colourless prisms, m. p. 126—128°, readily soluble in water to a golden-yellow solution (Found : C, 63·5; H, 8·6; N, 8·9; Cl, 14·6. $C_{25}H_{40}ON_3Cl,HCl$ requires C, 63·8; H, 8·7; N, 8·9; Cl, 15·1%). Antimalarial activity was observed only with the maximum tolerated dose.

The free base was a pale yellow, uncrystallisable oil. The meconate, prepared in the usual way, was an orange-red solid which was not investigated, as it was almost insoluble in water. A crude specimen had m. p. 141—142°. The dihydrochloride, precipitated from a solution of the base in ether in the usual manner, was a viscous red oil.

8-ω-Carboxydecylamino-6-methoxyquinoline and Derivatives.—Ethyl ester. Ethyl 11-bromoundecoate (62 g.) and 8-amino-6-methoxyquinoline (55 g.) were heated together at 120—130° for 12 hours. The mass was thoroughly triturated and washed with ether; the solid material was aminomethoxyquinoline hydrobromide (18 g. of the base

recovered). The ethereal solution was shaken with dilute hydrochloric acid; the yellow hydrochloride that separated was collected, washed with ether and with hot water, and triturated with aqueous sodium carbonate. The free *base*, isolated by means of ether (yield, 34 g.), after several crystallisations from alcohol, had m. p. 43—47°, not raised by recrystallisation (Found: C, 71·2; H, 8·9; N, 7·3. $C_{23}H_{34}O_2N_2$ requires C, 71·5; H, 8·8; N, 7·3%). This ester was recovered unchanged (m. p. and mixed m. p.) after being heated with saturated ethyl-alcoholic ammonia for 7 hours at 95—100° in a sealed tube (Found: N, 7·5%).

The acid. The above ester (20 g.) was refluxed for 2 hours on the steam-bath with alcoholic potassium hydroxide (1200 c.c. of 5%). Most of the alcohol was distilled, and concentrated hydrochloric acid added in slight excess, followed by aqueous sodium carbonate just to neutralise mineral acid (Congo-red). The buff-coloured precipitate was collected, washed with water, dried, and crystallised from alcohol (yield, 14 g., 75%), forming pale yellow, prismatic needles, m. p. 110—111°, soluble in aqueous acids and alkalis (Found: C, 70·7; H, 8·2; N, 7·8. $C_{21}H_{30}O_3N_2$ requires C, 70·4; H, 8·4; N, 7·8%).

The amide. Thionyl chloride (7 c.c.), dissolved in benzene (10 c.c.), was gradually added to a suspension of the acid (3·6 g.) in benzene (110 c.c.) cooled in ice-salt and efficiently agitated. The temperature was then raised to 40° and maintained until evolution of sulphur dioxide ceased. The mixture was cooled to 0° and slowly added with vigorous stirring to a large excess of aqueous ammonia (*d* 0·88) cooled to − 10°. The *amide* was precipitated as a pale yellow solid which tended to become green on standing; it was collected, thoroughly washed with water, dried, and crystallised from alcohol, forming buff-coloured prisms, m. p. 113—114° (yield, 30%) (Found: C, 70·9; H, 8·8; N, 12·0. $C_{21}H_{31}O_2N_3$ requires C, 70·6; H, 8·7; N, 11·8%).

An attempt to prepare the related nitrile by dehydration with phosphoric oxide in benzene solution was unsuccessful.

8-*ω*-*Cyanodecylamino*-6-*methoxyquinoline*.—A mixture of 8-amino-6-methoxyquinoline (17·4 g.) and 11-bromoundeconitrile (24·6 g.) (Trunel, *Compt. rend.*, 1933, **197**, 435) was heated at 110—120° for 17 hours under nitrogen. The melt gradually solidified to an orange-yellow crystalline mass. After cooling, it was triturated with ether, and the solid material (8-amino-6-methoxyquinoline hydrobromide) collected and washed with ether. When the ethereal extract and washings were concentrated, the condensation product separated; it was collected and washed with ether (yield, 7 g., 38%, allowing for 8 g. of recovered aminomethoxyquinoline). 8-*ω*-*Cyanodecylamino*-6-*methoxyquinoline* crystallised from alcohol in colourless prisms, m. p. 84—85° (Found: C, 74·5; H, 8·8; N, 12·3. $C_{21}H_{29}ON_3$ requires C, 74·4; H, 8·6; N, 12·4%).

8-*ω*-*Guanyldecylamino*-6-*methoxyquinoline* (R. 101).—A mixture of powdered cyanodecylaminomethoxyquinoline (3·4 g.), alcohol (1·4 c.c.), and light petroleum (50 c.c.) was saturated with hydrogen chloride at − 5°, and the solid occasionally broken up until all the orange-red material had disappeared. The vessel was then stoppered securely and kept in a refrigerator for 4 weeks. The solvent was decanted, and the residue freed from hydrogen chloride and light petroleum under diminished pressure. The imino-ether hydrochloride was pulverised, mixed with an excess of saturated ethyl-alcoholic ammonia, and heated in a sealed vessel at 40—50° for 6 hours. When cold, the alcoholic solution of the amidine was separated from ammonium chloride, and the ammonia and alcohol removed under reduced pressure. The residue was rubbed with ether, collected, dried, and triturated with a little chilled alcohol. The readily soluble amidine hydrochloride was precipitated by the addition of a large volume of dry ether to the filtered solution. This procedure was repeated twice, and the *product* finally crystallised from a little water, from which it separated in small, buff-coloured, prismatic needles (3 g.), m. p. 76—77° (Found: N, 13·4. $C_{21}H_{33}ON_3,HCl,H_2O$ requires N, 13·5%). The salt was dehydrated at 30—40° (Found: C, 64·5; H, 8·7; N, 14·3. $C_{21}H_{33}ON_3,HCl$ requires C, 64·2; H, 8·4; N, 14·3%).

R. 101 showed no antimalarial action at the M.T.D. of 6 × 10·24 mg. It was weakly active against trypanosomes in mice (Warrington Yorke).

8-*ω*-*Cyanodecylaminoquinoline*.—A mixture of 8-aminoquinoline (9 g.) and 11-bromoundeconitrile (12 g.) was heated for 24 hours at 110—120° under nitrogen. The orange-red condensate was thoroughly triturated and washed with ether, and then repeatedly extracted with hot water until the extracts were almost colourless. The dark red, viscous residue solidified on cooling, and was pulverised and triturated with cold aqueous sodium carbonate. The greyish-yellow, thick gum eventually solidified (5 g.). It crystallised from alcohol in small, greyish-yellow prisms, m. p. 60—61° (Found: C, 77·8; H, 8·6; N, 13·8. $C_{20}H_{27}N_3$ requires C, 77·6; H, 8·7; N, 13·6%).

8-*ω*-*Guanyldecylaminoquinoline*.—The preparation was like that of guanyldecylaminomethoxyquinoline, and the resulting base resembled its 6-methoxy-derivative in physical and chemical properties. The *hydrochloride* separated from alcohol in small, almost colourless, prismatic needles, m. p. 92—93° (Found: C, 66·5; H, 8·8; N, 15·5. $C_{20}H_{30}N_4,HCl$ requires C, 66·2; H, 8·5; N, 15·5%).

8-*γ*-*Cyanopropylaminoquinoline*.—Equivalent quantities of 8-aminoquinoline and *γ*-bromobutyronitrile were heated together at 90° under nitrogen for 12 hours, and the temperature then raised to 100—110° for a further 12 hours. The orange-red product was washed with ether and crystallised from alcohol. The *base* was liberated and repeatedly crystallised from alcohol; it formed small, grey prisms, m. p. 52—53° (Found: C, 74·2; H, 6·4; N, 19·9. $C_{13}H_{13}N_3$ requires C, 73·9; H, 6·2; N, 19·9%).

8-*γ*-*Guanylpropylaminoquinoline*.—The preparation from the cyanopropylaminoquinoline was like that described above. The *hydrochloride* crystallised from alcohol in small, colourless prisms which darkened at 148°, m. p. 152—154° (Found: C, 58·8; H, 6·4; N, 21·1. $C_{13}H_{16}N_4,HCl$ requires C, 59·0; H, 6·4; N, 21·2%).

ψ-6-*Amino*-2-p-*dimethylaminostyryl*-1-*γ*-*aminopropylquinolinium Bromide Hydrobromide* (V).—A mixture of 6-aminoquinaldine (16 g., m. p. 185—186°, by reduction of 6-nitroquinaldine with stannous chloride and hydrochloric acid) and acetic anhydride (20 g.) was heated for 20 minutes on the steam-bath. 6-Acetamidoquinaldine (18 g.) was crystallised from much boiling water. The product was a hydrate, m. p. 90—100°; after drying at 70° the m. p. was 168—169°.

A solution of 6-acetamidoquinaldine (12 g.) and phthalo-*γ*-bromopropylimide (20 g.) in nitrobenzene (20 c.c.) was heated for 7 hours at 120—130°. The product was cooled, washed with ether, refluxed with alcohol, and collected from the hot mixture (13 g.). This quaternary salt, crystallised from a mixture of alcohol (75 c.c.) and water (25 c.c.), formed pale yellow prisms which darkened at 235—240°, m. p. 240—245° (decomp.) (Found: C, 58·9; H, 4·9; N, 8·7; Br, 16·8. $C_{32}H_{31}O_3N_3Br$ requires C, 58·9; H, 4·7; N, 9·0; Br, 17·1%). A mixture of *ψ*-6-*acetamido*-2-*methyl*-1-*γ*-*phthalimidopropylquinolinium bromide* (4·7 g.), *p*-dimethylaminobenzaldehyde (2 g.), alcohol (200 c.c.), water (10 c.c.), and a few drops of piperidine was refluxed for 9 hours. The solution became deep purple, and a dark red crystalline solid separated. The product was collected from the hot solution, thoroughly washed with hot alcohol, and dried (3 g.) (Found: C, 64·1; H, 5·2; N, 9·3; Br, 12·8. $C_{32}H_{31}O_3N_4Br$ requires C, 64·1; H, 5·2; N, 9·4; Br, 13·3%).

A mixture of this *ψ*-6-*acetamido*-2-p-*dimethylaminostyryl*-1-*γ*-*phthalimidopropylquinolinium bromide* (4·0 g.), water (50 c.c.), and hydrobromic acid (55 c.c. of 48%) was gently refluxed for 8 hours, and the solution cooled, filtered, and evaporated to dryness on the steam-bath. The residue was extracted with boiling chloroform, dried, extracted with a little hot alcohol, and collected. The *bromide hydrobromide*, crystallised twice from aqueous alcohol, formed dark purple prisms, which were freely soluble in water (Found: C, 51·9; H, 5·6; N, 11·3; Br, 30·6. $C_{32}H_{32}N_4Br,HBr$ requires C, 51·9; H, 5·5; N, 11·0; Br, 31·5%). This salt (R. 100) showed no antimalarial activity at the M.T.D. of 6 × 10 mg.

The following is reported by Professor C. H. Browning, F.R.S. Antiseptic properties: *Staphylococcus*; 1 : 20,000

inhibits in peptone water; 1 : 40,000 inhibits in serum. *B. coli*; 1 : 40,000 inhibits in peptone water; 1 : 100,000 inhibits in serum. Trypanocidal action in mice infected with *T. brucei*: 1 : 1000 may cure; the blood is slowly cleared of trypanosomes after treatment; 1 : 20,000 has only slight action.

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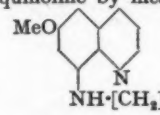
149. *Attempts to find New Antimalarials. Part XX.*

By (MISS) J. CRUM and SIR ROBERT ROBINSON.

Up to the present the basic side-chain in antimalarials of the plasmoquin (pamaquin) type has terminated with a primary or tertiary amine group. The present investigation was undertaken with the object of including *sec.*-amine end-groups in the series.

A general method has been devised for this purpose which consists in alkylation of 8-amino-6-methoxyquinoline by means of a chlorohydrin, replacement of the hydroxyl group in the product by chlorine, and reaction of the chloroalkylamino-compound with primary bases. The method can naturally also be used for *tert.*-bases by employing *sec.*-bases at the last stage.

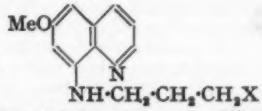


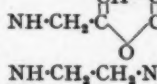
The general formula of bases allied to plasmoquin that can be conveniently prepared in this way is annexed and in the present communication we explore the series where $x = 3$.

CONDENSATION of 8-amino-6-methoxyquinoline and trimethylenechlorohydrin affords *8-γ-hydroxypropylamino-6-methoxyquinoline*, $MeO{\cdot}C_9H_5N{\cdot}NH{\cdot}[CH_2]_3{\cdot}OH$ (I), which is converted by thionyl chloride into the corresponding *chloride*, $MeO{\cdot}C_9H_5N{\cdot}NH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Cl$ (II). A red by-product is always produced and this becomes the sole product if the reaction with thionyl chloride is at all prolonged, for example, to ½ hour; the substance is very probably the *hydrochloride* of *bis-(8-γ-chloropropylamino-6-methoxy-5-quinolyl) sulphide*; the free base is crystalline. Reaction with diethylamine gives a thio-bis-rhodoquin, $S(MeO{\cdot}C_9H_4N{\cdot}NH{\cdot}[CH_2]_3{\cdot}NEt_2)_2$ (III), the first member of a group capable of considerable extension.

Reaction of (II) with various primary and secondary bases has given a series of antimalarials showing interesting variations of activity.

The following results of tests on bird malaria due to *Plasmodium relictum* in canaries of some of the compounds described in this paper have been received from Professor D. Keilin, F.R.S., and Dr. Ann Bishop, of the Molteno Institute, Cambridge. In each case the dose was given on six successive days.



Number in R series.	X.	Max. tolerated dose in mg. per 20 g. of body weight.	Min. effective dose in mg. per 20 g. of body weight.	Therapeutic index.
105	NHMe	2·56	0·32	1/8
106	NHEt	0·16	0·04	1/4
119	NHPr$^{\alpha}$	0·64	0·04	1/16
108	NHPr$^{\beta}$	0·32	0·02	1/16
107	NH-*n*-C_4H_9	0·32	0·04	1/8
110	NH-*iso*-C_4H_9	0·16	0·02	1/8
109	NH-*tert.*-C_4H_9	0·32	0·01	1/32
114	NH-*n*-C_7H_{15}	0·64	0·16	1/4
117	NH·CH_2Ph	0·32	0·08	1/4
111	NH·CHMe·CH_2Ph	0·32	0·16—0·08	1/2—1/4
112		0·32	0·02	1/16
115	NH·CH_2·CH_2·NH_2	5·12	2·56	1/2
116	NEt_2	0·32	0·02	1/16
120	NH·$[CH_2]_3$·NH_2		(Inactive)	

The new synthesis of 8-γ′-aminopropyl-γ-aminopropyl-6-methoxyquinoline,

$$MeO{\cdot}C_9H_5N{\cdot}NH{\cdot}[CH_2]_3{\cdot}NH{\cdot}[CH_2]_3{\cdot}NH_2$$

from (II) and trimethylenediamine confirms that of Part XVIII. The substance is reported as devoid of antimalarial properties and it is now certain that R. 63 owes its activity to some other constituent.

EXPERIMENTAL.

8-Amino-6-methoxyquinoline.—8-Nitro-6-methoxyquinoline (102 g.) was hydrogenated in methyl alcohol (200 c.c.) for 1 hour at 60°/80 atm. in presence of a Raney nickel catalyst. The product, b. p. 162°/0·2 mm., crystallised in almost colourless prisms, m. p. 41° (83 g., 95%).

8-γ-Hydroxypropylamino-6-methoxyquinoline (I).—A mixture of 8-amino-6-methoxyquinoline (58 g.), trimethylenechlorohydrin (32 g.), finely powdered potassium carbonate (25 g.), and octyl alcohol (about 3 c.c.) was refluxed (bath, 125—130°) for 10 hours and then added to water and extracted with chloroform. On distillation a small amount of

unchanged material was recovered. The *product* (59 g., 76%) was a pale yellow oil, b. p. 200°/0·1 mm.; it crystallised, on keeping, in yellow prisms, m. p. 53° (Found : C, 67·1; H, 7·0. $C_{13}H_{16}O_3N_2$ requires C, 67·2; H, 6·9%).

The picrate crystallised from benzene in orange needles, m. p. 128°; the hydrogen oxalate crystallised from alcohol–ethyl acetate, containing oxalic acid, in yellow needles, m. p. 109°; the hydrochloride separated from alcohol as deliquescent orange needles, m. p. 178°.

8-*γ*-*Chloropropylamino*-6-*methoxyquinoline* (II).—Thionyl chloride (15 g., 3 mols.) was added to 8-*γ*-hydroxypropylamino-6-methoxyquinoline (10 g.) in chloroform (30 c.c.) at − 5°, and the mixture distilled from the steam-bath as rapidly as convenient. When the evolution of gases became less vigorous (3—5 minutes), saturated alcoholic hydrogen chloride (30 c.c.) was added, and the hot solution filtered from a red by-product, traces of which were always formed in the reaction. On cooling, the hydrochloride crystallised from the filtrate in brown needles. A further crop was obtained by washing the by-product with boiling alcohol and by evaporating the combined mother-liquors. After boiling with charcoal in alcoholic solution and several recrystallisations from alcohol–ethyl acetate the hydrochloride was obtained as orange needles, m. p. 180° (7·4 g., 60%). It was converted into the free *base*, which distilled as a yellow oil, bath at 115°/0·0001 mm. (Found : C, 62·1; H, 5·8. $C_{13}H_{15}ON_2Cl$ requires C, 62·3; H, 6·0%). Even under these conditions a considerable amount of decomposition occurred and the more satisfactory means of purification was recrystallisation of the hydrochloride and passage of a solution of the free base in chloroform through an alumina column.

The picrate separated from benzene in orange needles, m. p. 128°.

Bis-(8-*γ*-*chloropropylamino*-6-*methoxy*-5-*quinolyl*) *Sulphide*.—The red by-product, mentioned above, was formed in amounts varying with the conditions under which the reaction was carried out. If the reactants were refluxed together for ½ hour or more, it was obtained in practically theoretical yield. Since it was extremely sparingly soluble in all solvents, it could not be purified directly, but was converted into the free *base* by means of aqueous ammonia. This crystallised from alcohol–benzene in fine, yellow needles, m. p. 144°, readily soluble in benzene, sparingly soluble in alcohol, ether and ethyl acetate, and almost insoluble in water and light petroleum (Found : C, 58·9; H, 5·1; N, 10·6; Cl, 13·1; S, 6·3; active H, 0·38. $C_{26}H_{28}O_2N_4Cl_2S$ requires C, 58·8; H, 5·3; N, 10·6; Cl, 13·4; S, 6·0; 2H, 0·38%). On heating with camphor, decomposition occurred so that a Rast determination of the molecular weight could not be carried out. Attempted benzoylation and acetylation did not give crystalline derivatives.

Hydrochloride. The free base, dissolved in benzene, was mixed with an excess of ethereal hydrogen chloride; the finely divided, deliquescent, red precipitate was separated centrifugally, washed with ethyl acetate, and again centrifuged, and the process repeated until the washings were no longer acid; it was then dried in a desiccator; m. p. 200—201° (Found : C, 47·6; H, 5·6; Cl, 21·3. $C_{26}H_{28}O_2N_4Cl_2S,2HCl,3H_2O$ requires C, 47·4; H, 5·5; Cl, 21·5%). Attempts to crystallise the salt were unsuccessful, as on boiling with water or alcohol hydrolysis occurred and the free base was formed.

Bis-(8-*γ*-*diethylaminopropylamino*-6-*methoxy*-5-*quinolyl*) *Sulphide* (III) (R. 118, index 1 : 7—1 : 8).—Bis-(8-*γ*-chloropropylamino-6-methoxy-5-quinolyl) sulphide (10 g.) was heated with a large excess of diethylamine (10 g.) in a sealed tube at 120—125° for 12 hours. The product was treated with aqueous sodium carbonate, and the excess of diethylamine removed by distillation. The *product* (9·1 g., 80%) crystallised from benzene–light petroleum in stout yellow needles, m. p. 85° (Found : C, 67·2; H, 8·0; N, 14·0; OMe, 9·8. $C_{34}H_{48}O_2N_6S$ requires C, 67·2; H, 7·9; N, 13·9; 2OMe, 10·2%). The meconate separated from alcohol–ethyl acetate in yellow polyhedra, m. p. 140° (decomp.); the picrate crystallised from alcohol in yellow prisms, m. p. 173° (decomp.) (evacuated capillary).

The *hydrochloride* was a deliquescent, orange, micro-crystalline powder, m. p. 150° (decomp.) (Found : C, 53·1; H, 7·3; N, 10·7; Cl, 18·3. $C_{34}H_{48}O_2N_6S,4HCl,H_2O$ requires C, 53·1; H, 7·3; N, 10·7; Cl, 18·5%). It crystallised from alcohol–ethyl acetate but owing to its deliquescent nature and fine state of division it was necessary to remove the mother-liquor and to wash the solid by centrifuging and decantation. An attempt to remove the water of crystallisation by heating at 100° in a vacuum over phosphoric oxide resulted in decomposition.

Condensation of 8-*γ*-*Chloropropylamino*-6-*methoxyquinoline with Primary and Secondary Amines*.—The chloro-compound was heated with a large excess of the amine in sealed tubes at 125—135° for 7—12 hours.

8-*γ*-*Methylaminopropylamino*-6-*methoxyquinoline* (R. 105). The reaction product was treated with dilute aqueous sodium carbonate and extracted with ether. The ether and excess of methylamine were evaporated; the residual oil had b. p. 166°/0·5 mm. (Found : C, 68·6; H, 7·9. $C_{14}H_{19}ON_3$ requires C, 68·6; H, 7·8%). Some decomposition occurred on distillation, and crystallisation of the *hydrogen oxalate* was found to be a better method of purification. This derivative separated from ethyl acetate–alcohol, containing oxalic acid, in yellow prisms, m. p. 188° (Found : C, 50·7; H, 5·5. $C_{14}H_{19}ON_3,2C_2H_2O_4$ requires C, 50·8; H, 5·4%).

The *hydrochloride* was prepared in ethereal solution and washed with ether. It crystallised from alcohol in deliquescent, orange needles, m. p. 218° (Found : C, 52·5; H, 6·9; N, 12·9. $C_{14}H_{19}ON_3,2HCl$ requires C, 52·8; H, 6·6; N, 13·2%).

8-*γ*-*Ethylaminopropylamino*-6-*methoxyquinoline* (R. 106). As in the last case, the excess of amine was removed by distillation with ether. The *hydrogen oxalate*, purified by several crystallisations from alcohol–ethyl acetate mixtures containing oxalic acid, formed yellow prisms, m. p. 139° (Found : C, 51·5; H, 5·8. $C_{15}H_{21}ON_3,2C_2H_2O_4$ requires C, 51·9; H, 5·7%). The free base was obtained from the pure oxalate by the action of aqueous sodium carbonate; its solution in chloroform was passed through an alumina column and evaporated. The *hydrochloride*, prepared by means of ethereal hydrogen chloride, crystallised from alcohol–ethyl acetate in deliquescent, orange needles, m. p. 206° (Found : C, 51·8; H, 7·0. $C_{15}H_{21}ON_3,2HCl,H_2O$ requires C, 51·5; H, 7·1%).

n-*Propylamine*. Propionitrile (55 g.) was hydrogenated in alcoholic ammonia (200 c.c., saturated at 0°) for 4 hours at 100—150°/100 atm., a Raney nickel catalyst being used. The product was worked up through the hydrochloride, and the free bases fractionated, b. p. 49—52°/748 mm. (45 g., 75%). *n*-Propylamine picrate formed yellow needles from alcohol, m. p. 132—134° (lit. 135°).

8-*γ*-*Propylaminopropylamino*-6-*methoxyquinoline* (R. 119). The excess of propylamine was removed by distillation in a stream of chloroform, and the *hydrogen oxalate* prepared and purified by several crystallisations from alcohol containing oxalic acid. It formed golden-yellow plates, m. p. 173° (Found : C, 52·7; H, 6·1. $C_{16}H_{23}ON_3,2C_2H_2O_4$ requires C, 53·0; H, 6·0%). A solution of the free base in chloroform was passed through an alumina column. The *hydrochloride* crystallised from alcohol in deliquescent, golden-orange plates, m. p. 162° (Found : C, 55·3; H, 7·3. $C_{16}H_{23}ON_3,2HCl$ requires C, 55·5; H, 7·2%).

iso*Propylamine*. Acetoxime (73 g.) was hydrogenated for 3 hours in alcoholic ammonia (100 c.c., saturated at 0°) at 90—130°/60 atm., a Raney nickel catalyst being used. *iso*Propylamine (30 g., 50%), b. p. 32°, was obtained by way of the mixture of hydrochlorides; the benzenesulphonamide had m. p. 98° (lit. 99°).

8-*γ*-iso*Propylaminopropylamino*-6-*methoxyquinoline* (R. 108). The excess of *iso*propylamine was removed by distillation with chloroform, and the *hydrogen oxalate* prepared and purified by several crystallisations from aqueous alcohol containing oxalic acid. It formed golden plates, m. p. 136° (Found : C, 53·0; H, 6·0. $C_{16}H_{23}ON_3,2C_2H_2O_4$ requires C, 53·0; H, 6·0%). The meconate crystallised from aqueous alcohol in golden plates, m. p. 195°. The *hydrochloride* crystallised from alcohol in well-formed yellow needles, m. p. 210° (Found : C, 55·8; H, 7·1. $C_{16}H_{23}ON_3,2HCl$ requires C, 55·5; H, 7·2%).

8-γ-n-*Butylaminopropylamino*-6-*methoxyquinoline* (R. 107). After removal of the excess of *n*-butylamine by distillation with chloroform the *hydrogen oxalate* was prepared. It crystallised from alcohol, containing oxalic acid, in small, yellow needles, m. p. 141° (Found: C, 52·3; H, 6·2; N, 8·3. $C_{17}H_{25}ON_3,2C_2H_2O_4,H_2O$ requires C, 52·0; H, 6·4; N, 8·7%). The *picrate* crystallised from much alcoholic picric acid as a pale yellow, microcrystalline powder, m. p. 178° (Found: N, 17·1. $C_{17}H_{25}ON_3,2C_6H_3O_7N_3$ requires N, 16·9%). The *hydrochloride* crystallised from alcohol–ethyl acetate in deliquescent orange needles, m. p. 180° (Found: C, 54·2; H, 7·5. $C_{17}H_{25}ON_3,2HCl,H_2O$ requires C, 53·9; H, 7·7%). The anhydrous salt, obtained by heating the monohydrate at 60° in a vacuum over phosphoric oxide for 12 hours, crystallised from alcohol as a microcrystalline, buff-coloured powder, m. p. 79° (evacuated capillary). It rapidly took up moisture from the atmosphere, becoming orange.

8-γ-iso*Butylaminopropylamino*-6-*methoxyquinoline* (R. 110). The excess of *iso*butylamine was removed by evaporation with benzene. The *hydrogen oxalate* crystallised from aqueous alcohol in lustrous buff-coloured plates, m. p. 218° (Found: C, 58·6; H, 6·9; N, 10·6. $C_{17}H_{25}ON_3,C_2H_2O_4,H_2O$ requires C, 58·9; H, 7·1; N, 10·3%). The *hydrochloride* was precipitated as an oil but crystallised, on keeping, in orange needles, m. p. 192—195°. On heating at 60° in a vacuum over phosphoric oxide for several days, the anhydrous form was obtained, m. p. 178° after crystallisation from alcohol–ethyl acetate (Found: C, 56·4; H, 7·6; N, 11·7. $C_{17}H_{25}ON_3,2HCl$ requires C, 56·7; H, 7·5; N, 11·7%).

8-γ-tert.-*Butylaminopropylamino*-6-*methoxyquinoline* (R. 109). The excess of *tert.*-butylamine was removed by distillation with chloroform. The *meconate*, crystallised from aqueous alcoholic meconic acid, formed yellow prisms, m. p. 188° (Found: C, 54·1; H, 5·0. $C_{17}H_{25}ON_3,2C_7H_4O_7$ requires C, 54·1; H, 4·8%). The hydrogen oxalate crystallised from alcohol in orange needles, m. p. 184°. The *hydrochloride* crystallised from alcohol in pinkish-orange needles, m. p. 174° (Found: C, 57·0; H, 7·7; N, 12·1. $C_{17}H_{25}ON_3,2HCl$ requires C, 56·7; H, 7·5; N, 11·7%).

n-*Heptylamine*. *n*-Heptaldehyde (57 g.) was mixed with alcoholic ammonia (300 c.c., saturated at 0°), considerable heat being evolved. The mixture was hydrogenated for 3 hours at 90—130°/60 atm., a Raney nickel catalyst being used. *n*-Heptylamine was obtained as a colourless liquid, b. p. 153°/756 mm. (34 g., 60%); the picrate formed yellow needles from alcohol, m. p. 121° (lit. 120—122°).

8-γ-n-*Heptylaminopropylamino*-6-*methoxyquinoline* (R. 114). The excess of *n*-heptylamine was removed by steam distillation in a vacuum. A solution of the free base in chloroform was passed through an alumina column and evaporated, and the *hydrogen oxalate* prepared. It crystallised from alcohol in lustrous yellow needles, m. p. 181° (Found: C, 56·7; H, 7·2. $C_{20}H_{31}ON_3,2C_2H_2O_4$ requires C, 56·6; H, 6·9%). The free base was again purified by means of an alumina column, and the *hydrochloride* precipitated in ethereal solution. It crystallised, on standing, in deliquescent orange needles which darkened in the air, m. p. 110—112° (Found in material dried at 60° in a high vacuum: C, 59·7; H, 8·3; N, 10·4. $C_{20}H_{31}ON_3,2HCl$ requires C, 60·0; H, 8·4; N, 10·5%).

8-γ-*Benzylaminopropylamino*-6-*methoxyquinoline* (R. 117). The excess of benzylamine was removed by steam distillation in a vacuum, a chloroform solution of the free base passed through an alumina column and evaporated and the *hydrogen oxalate* prepared. It crystallised from aqueous alcoholic oxalic acid in golden plates, m. p. 230° (Found: C, 62·8; H, 6·2; N, 9·3; OMe, 7·0. $C_{20}H_{23}ON_3,C_2H_2O_4,C_2H_2O$ requires C, 63·0; H, 6·8; N, 9·2; 1OMe, 6·8%). The *hydrochloride* crystallised from alcohol in fine, yellow needles, m. p. 204° (Found: C, 59·7; H, 6·7; Cl, 17·3. $C_{20}H_{23}ON_3,2HCl,\frac{1}{2}H_2O$ requires C, 59·6; H, 6·5; Cl, 17·6%).

8-β′-*Phenylisopropyl*-γ-*aminopropylamino*-6-*methoxyquinoline* (R. 111). The excess of β-phenyl*iso*propylamine was removed by steam distillation in a vacuum. A solution of the free base in chloroform was passed through an alumina column and evaporated, and the *hydrogen oxalate* prepared. It crystallised from aqueous alcoholic oxalic acid in fine, buff-coloured needles, m. p. 128° (Found: C, 63·2; H, 6·4; N, 9·3. $C_{22}H_{27}ON_3,C_2H_2O_4,H_2O$ requires C, 63·2; H, 6·4; N, 9·2%). The *hydrochloride* crystallised from alcohol–ethyl acetate in deliquescent, yellow needles, m. p. 127° (Found: C, 62·4; H, 7·1. $C_{22}H_{27}ON_3,2HCl$ requires C, 62·6; H, 6·9%).

cyclo*Hexylamine*. *cyclo*Hexanoneoxime (56·5 g.) was hydrogenated for 3 hours in alcoholic ammonia (200 c.c., saturated at 0°) at 90—130°/80 atm., a Raney nickel catalyst being used. *cyclo*Hexylamine, b. p. 134°/762 mm. (56 g., 56%), was obtained on fractionation of the bases obtained by way of the hydrochlorides; hexahydrobenzanilide formed colourless needles from alcohol, m. p. 147° (*lit.* 147°).

8-γ-cyclo*Hexylaminopropylamino*-6-*methoxyquinoline*. The excess of *cyclo*hexylamine was removed by steam distillation in a vacuum. A solution of the free base in chloroform was passed through an alumina column and evaporated, and the *hydrogen oxalate* prepared. It crystallised from alcoholic oxalic acid in buff-coloured prisms, m. p. 215° (Found: C, 62·6; H, 7·2; N, 10·0. $C_{19}H_{27}ON_3,C_2H_2O_4$ requires C, 62·5; H, 7·1; N, 10·4%). The yield in this case was very poor and the hydrochloride has not, as yet, been prepared.

8-γ-*Furfurylaminopropylamino*-6-*methoxyquinoline* (R. 112). The *hydrogen oxalate* was prepared like previous examples and purified by several crystallisations from aqueous alcoholic oxalic acid. It formed buff-coloured prisms, m. p. 209° (Found in material dried at 80° in a high vacuum: C, 58·6; H, 5·9. $C_{18}H_{21}O_2N_3,C_2H_2O_4,H_2O$ requires C, 58·5; H, 5·6%). The *hydrochloride* crystallised from alcohol–ethyl acetate in fine, deliquescent, yellow needles, m. p. 203° (Found: C, 55·6; H, 6·7; N, 9·9. $C_{18}H_{21}O_2N_3,2HCl,C_2H_4O$ requires C, 55·8; H, 6·7; N, 9·8%). There was no loss in weight on heating at 80° over phosphoric oxide in a high vacuum for several days.

8-β′-*Aminoethyl*-γ-*aminopropylamino*-6-*methoxyquinoline* (R. 115). The excess of ethylenediamine was removed by steam distillation in a vacuum. The alkaline solution was then continuously extracted with chloroform for 3 hours, and the chloroform solution passed through an alumina column. After evaporation the *hydrogen oxalate* was prepared. It crystallised from aqueous oxalic acid in yellow prisms, m. p. 221° (Found: C, 43·9; H, 4·8; N, 8·9. $C_{15}H_{22}ON_4,4C_2H_2O_4$ requires C, 43·5; H, 4·7; N, 8·8%). The *meconate* crystallised from aqueous alcoholic meconic acid in light orange prisms, m. p. 186° (decomp.) (Found: C, 48·3; H, 5·6; N, 7·7. $C_{15}H_{22}ON_4,3C_7H_4O_7,3H_2O$ requires C, 48·5; H, 5·0; N, 7·7%). An attempt to obtain the anhydrous form by heating at 100° in a high vacuum over phosphoric oxide resulted in decomposition. The *hydrochloride* crystallised from aqueous alcohol in deliquescent, orange needles, m. p. 244°. (Found: C, 46·5; H, 6·5; N, 14·7. $C_{15}H_{22}ON_4,3HCl$ requires C, 46·9; H, 6·5; N, 14·6%).

Trimethylenediamine. The methods available for the preparation of this base have been compared and the best is probably the application of the Hofmann reaction to glutardiamide.

(*a*) Hydrolysis of 1 : 3-diphthalimidopropane by means of hydrazine hydrate gave a product contaminated with hydrazine, from which it was not possible to separate it by distillation.

(*b*) By the method of Gabriel and Weiner (*Ber.*, 1888, **21**, 2670) diphthalimidopropane (56 g.) gave 6 g. (58%), b. p. 135°, of the anhydrous base; dipicrate, yellow needles, m. p. 248° (decomp.) (lit. 250°).

(*c*) An attempt was made to hydrogenate malononitrile in alcoholic ammonia with a Raney nickel catalyst at 90—130°/80 atm., but before the theoretical volume of hydrogen had been absorbed large quantities of solid separated which prevented further stirring and it was obvious that the nitrile had polymerised.

(*d*) (cf. Galat and Elion, *J. Amer. Chem. Soc.*, 1939, **61**, 3585). Condensation of hexamine with trimethylene dibromide in aqueous alcoholic solution in presence of sodium iodide gave sticky resin. The method did not appear to be promising.

(*e*) (cf. Aspinall, *J. Amer. Chem. Soc.*, 1941, **63**, 2843). After trial of other methods, glutardiamide was prepared as follows. Glutaryl dichloride was added gradually, with good stirring, to a mixture of ether (500 c.c.) and aqueous

ammonia (500 c.c., *d* 0·880) cooled to 0°. The solution was evaporated to dryness under reduced pressure and the mixture of ammonium chloride and glutardiamide was extracted several times with boiling amyl alcohol. On cooling, the glutardiamide separated as a buff-coloured, micro-crystalline powder, m. p. 168° (26 g., 61%). After several crystallisations (charcoal) from boiling amyl alcohol it formed colourless plates, m. p. 176° with evolution of gas (lit. 176°) (22 g., 50%). Bromine (160 g.) was gradually added to a solution of potassium hydroxide (280 g.) in water (750 c.c.) at 0°. Glutardiamide (65 g.) was introduced, and the temperature allowed to rise, and kept at 60° for 2 hours. The mixture was then steam-distilled, and the base in the distillate estimated by the gradual addition of hydrochloric acid (methyl-orange) (base, 29 g., 78%). The neutralised distillate was evaporated to dryness, the residue treated with excess of saturated aqueous potassium hydroxide, and aqueous trimethylenediamine distilled; it was dried over potassium hydroxide, and later sodium, and distilled (20 g. of anhydrous base, 54%).

(*f*) Sodium azide (3·2 g.) was mixed with warm water (4 c.c.) and chloroform (10 c.c.), then cooled to 0°, and concentrated sulphuric acid (2·5 g.) added gradually with good stirring below 5°. The organic layer was decanted and dried over sodium sulphate. This solution was added gradually to one of glutaric acid (2·64 g.) in concentrated sulphuric acid (5 c.c.) and chloroform (5 c.c.) at 43—45° with good stirring until carbon dioxide and nitrogen were no longer evolved. The mixture was then added to ice and neutralised, and the trimethylenediamine isolated as the dipicrate, m. p. 250° (9·6 g. of dipicrate or 0·96 g. of base, 65%). When an attempt was made to carry out the reaction on a larger scale (0·5 g.-mol.), the yield was very much diminished.

8-*γ'-Aminopropyl-γ-aminopropylamino-6-methoxyquinoline* (R. 120). The excess of trimethylenediamine was removed by steam distillation in a vacuum. The alkaline solution was extracted continuously with chloroform for a considerable time, the free base being readily soluble in water, and the extract was passed through an alumina column, the solvent evaporated, and the *hydrogen oxalate* prepared. It crystallised from aqueous alcoholic oxalic acid in tiny, pale yellow needles, m. p. 221° (Found: C, 50·8; H, 6·0; N, 11·8; OMe, 6·5. $C_{16}H_{24}ON_4,2C_2H_2O_4$ requires C, 51·2; H, 6·0; N, 11·9; 1OMe, 6·6%). The oxalate was decomposed with aqueous sodium carbonate, and the base again extracted continuously with chloroform. The solution was passed through an alumina column, the chloroform distilled, and the basic oil mixed with ethereal hydrogen chloride. Two hydrochlorides were formed and separated by fractional crystallisation from aqueous alcohol. The main product was the *hydrochloride* of 8-*γ'-aminopropyl-γ-aminopropylamino-6-methoxyquinoline*; it crystallised in deliquescent, yellow needles, m. p. 225° (decomp.) (Found: C, 47·7; H, 6·8; N, 14·2; Cl, 25·7. $C_{16}H_{24}ON_4,3HCl,\frac{1}{2}H_2O$ requires C, 47·2; H, 6·9; N, 13·7; Cl, 26·2%). The second hydrochloride, which was formed in small relative amount, crystallised from alcohol in deliquescent, colourless needles, m. p. 173°. Analysis indicated that the alkylamino-side chain had been eliminated, but the substance has not yet been identified (Found: Cl, 18·1%).

8-*δ'-Amino*-n-*butyl-γ-aminopropylamino-6-methoxyquinoline* (R. 121). Tetramethylenediamine was prepared from adipic acid both by the Schmidt reaction (yield, 65%) and by the Hofmann reaction (yield, 72%). The methods used were those described above in the case of trimethylenediamine (cf. von Braun and Lemke, *Ber.*, 1922, **55**, 3526; 1934, **67**, 1059; Oesterlin, *Z. angew. Chem.*, 1932, **45**, 536; Adamson and Kenner, J., 1934, 842; Adamson, J., 1939, 1564); dipicrate, pale yellow prisms from water; on heating it turned brown at 250°, and decomposed at 250—255° (lit. 250—255°). The condensation and purification followed those of the lower homologue. The *hydrogen oxalate* crystallised from aqueous alcoholic oxalic acid in tiny, yellow prisms, m. p. 183—185° (Found: C, 50·3; H, 6·5. $C_{17}H_{26}ON_4,2C_2H_2O_4,H_2O$ requires C, 50·4; H, 6·4%). The picrate crystallised from aqueous picric acid in yellow plates, decomp. 194° (evacuated capillary). The *hydrochloride* crystallised from alcohol–ethyl acetate in deliquescent orange-yellow prisms, which on heating underwent some change, probably dehydration, at 125—132°, m. p. 210° (Found: C, 47·7; H, 6·9. $C_{17}H_{26}ON_4,3HCl,H_2O$ requires C, 47·5; H, 7·2%).

Pentamethylenediamine. Glutardinitrile (31 g.) was hydrogenated in alcoholic ammonia (300 c.c., saturated at 0°) for 8 hours at 110—150°/80 atms. with a Raney nickel catalyst. The base was distilled, dried over potassium hydroxide, and redistilled, b. p. 178—180°/750 mm. (24 g., 70%); dibenzoylcadaverine had m. p. 135° (lit. 135°).

8-*ε-Amino*-n-*amyl-γ-aminopropylamino-6-methoxyquinoline* (R. 122). The excess of cadaverine was removed by steam distillation in a vacuum and the alkaline solution was extracted six times with chloroform; the base appeared to be considerably less readily soluble in water than the lower homologues. The chloroform solution was passed through an alumina column, the chloroform removed, and the *hydrogen oxalate* prepared. It crystallised from aqueous alcoholic oxalic acid in small yellow prisms, m. p. 162° (Found: C, 49·4; H, 6·2. $C_{18}H_{28}ON_4,3C_2H_2O_4$ requires C, 49·1; H, 5·8%). The *hydrochloride* crystallised from alcohol in deliquescent, yellow needles, m. p. 196° (Found: C, 50·4; H, 7·4. $C_{18}H_{28}ON_4,3HCl$ requires C, 50·8; H, 7·3%).

8-*β-Hydroxyethyl-γ-aminopropylamino-6-methoxyquinoline.* Ethanolamine was removed by steam distillation in a vacuum, and the free base extracted continuously with chloroform for several hours. The chloroform solution was passed through an alumina column, then evaporated, and the *picrate* prepared. It crystallised from aqueous alcoholic picric acid in yellow needles, m. p. 159° (decomp.) (evacuated capillary) (Found: C, 44·2; H, 3·7; N, 17·1. $C_{15}H_{21}O_2N_3,2C_6H_3O_7N_3$ requires C, 44·2; H, 3·7; N, 17·2%). The picrolonate, m. p. 216° (decomp.) (evacuated capillary), and the styphnate, m. p. 172° (decomp.) (evacuated capillary), both crystallised in yellow needles from aqueous alcohol. The hydrogen oxalate, m. p. 72°, and meconate, m. p. 204°, did not crystallise well from any solvent and were unsuitable for purification purposes. Difficulty was experienced in the decomposition of the picrate because the free base was oxidised by the action of sodium picrate in alkaline solution. The deliquescent *hydrochloride* crystallised from alcohol–ethyl acetate in small, orange rhombs which on heating melted at 98°, resolidified, and melted finally at 154° (Found in material dried at 80° in a high vacuum: C, 51·6; H, 6·8; N, 11·9; Cl, 26·9. $C_{15}H_{21}O_2N_3,2HCl$ requires C, 51·7; H, 6·6; N, 12·1; Cl, 26·8%).

8-*γ-Diethylaminopropylamino-6-methoxyquinoline* (Rhodoquin, R. 116). The free base was distilled, b. p. 198°/1 mm. (Magidson and Strukow, *Arch. Pharm.*, 1933, **271**, 572). The picrate crystallised from alcohol in orange needles, m. p. 186° (lit. 190°). When crystallised from pure alcohol, the monomeconate, yellow needles, m. p. 133—134° (lit. 133—134°), was obtained; when crystallised from alcoholic meconic acid, the *dimeconate*, yellow needles, m. p. 178°, was isolated (Found: C, 54·2; H, 5·1; N, 6·2. $C_{17}H_{25}ON_3,2C_7H_4O_7$ requires C, 54·1; H, 4·8; N, 6·1%). The *hydrochloride* crystallised from alcohol in deliquescent yellow needles, m. p. 208° (Found: C, 56·4; H, 7·6; N, 11·7; Cl, 19·2. $C_{17}H_{25}ON_3,2HCl$ requires C, 56·7; H, 7·5; N, 11·7; Cl, 19·3%).

Methyl-*n*-propylamine was prepared by the action of formaldehyde on *n*-propylamine and reduction of the tripropyltrimethylenetriamine so formed with zinc and hydrochloric acid (Graymore, J., 1931, 1492). The method is said to give an almost quantitative yield of methylpropylamine; propylamine (8%) was, however, obtained as a by-product. The b. p. of tripropyltrimethylenetriamine, which is not recorded, is 170°/752 mm.

8-*γ-Methylpropylaminopropylamino-6-methoxyquinoline* (R. 123). The free base was distilled (bath at 115—120°/0·015—0·02 mm.) as a clear yellow oil. The *meconate* crystallised from alcoholic meconic acid in yellow needles, m. p. 168° (Found: C, 53·2; H, 4·7; N, 6·2. $C_{17}H_{25}ON_3,2C_7H_4O_7,H_2O$ requires C, 52·8; H, 4·9; N, 6·0%). The *picrate* separated from acetone–benzene as an orange, microcrystalline powder, m. p. 152—154° (decomp.) (evacuated capillary) (Found: C, 46·9; H, 4·1; N, 16·8. $C_{17}H_{25}ON_3,2C_6H_3O_7N_3$ requires C, 46·7; H, 4·2; N, 16·9%). The picrolonate separated from alcohol as a yellow microcrystalline powder, m. p. 128°. The *hydrochloride* crystallised from

aqueous alcohol in fine, orange needles, m. p. 180—184° (Found : C, 52·7; H, 7·5; N, 10·5. $C_{17}H_{25}ON_3,2HCl,1\frac{1}{2}H_2O$ requires C, 52·7; H, 7·8; N, 10·9%).

8-β-Hydroxyethylmethyl-γ-aminopropylamino-6-methoxyquinoline (R. 124). After steam distillation in a vacuum the base was extracted six times with chloroform. The *meconate* crystallised from aqueous alcoholic meconic acid in yellow needles, m. p. 128° (decomp.) (Found : C, 54·8; H, 5·9; N, 8·3. $C_{16}H_{23}O_2N_3,C_7H_4O_7,H_2O$ requires C, 54·4; H, 5·9; N, 8·0%). The *hydrochloride* crystallised from alcohol in fine, deliquescent, deep yellow needles, m. p. 212° (Found : C, 53·0; H, 6·8; N, 11·5; Cl, 19·8. $C_{16}H_{23}O_2N_3,2HCl$ requires C, 53·0; H, 6·9; N, 11·6; Cl, 19·6%).

Methylisopropylamine. A mixture of acetone (58 g.) and aqueous methylamine (200 c.c. of 33% w/v) was hydrogenated for 14 hours at 140—160°/60 atms. with a Raney nickel catalyst. The filtered solution was acidified with hydrogen chloride and evaporated to dryness. The mixture of hydrochlorides was then extracted several times with boiling chloroform, and the extracts evaporated. Methyl*iso*propylamine hydrochloride crystallised in colourless deliquescent needles, m. p. 71—74° (lit. 77°). Saturated potassium hydroxide solution was added, and the amine distilled, dried over potassium hydroxide, and redistilled, b. p. 50° (47 g., 65%); *N'*-phenyl-*N*-methyl-*N*-*iso*propylurea formed colourless needles from aqueous alcohol, m. p. 131°.

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150. *The Effect of Molecular Environment on the Absorption Spectra of Organic Compounds in Solution. Part III. Compounds containing the Chromophore* >C=C–C=N–.

By L. K. EVANS and A. E. GILLAM.

In continuation of earlier work on the absorption spectra of conjugated dienes and αβ-unsaturated ketones, the light absorption of various αβ-unsaturated aldehydes has been determined and discussed. Derivatives of carbonyl compounds containing the chromophore >C=C–C=N–, *i.e.*, semicarbazones, methylsemicarbazones, thiosemicarbazones, and oximes, have also been examined, and the data discussed with special reference to the detection of the >C=C–C=O group in organic molecules. It is shown that the thiosemicarbazones of *saturated* aldehydes and ketones exhibit absorption bands near 2700 A. which are some 500 times more intense than those of the parent carbonyl compound, thus providing an additional means of spectroscopic detection of the *isolated* carbonyl group.

THE primary factor determining the presence of a band in the absorption spectrum of an organic compound in solution is the occurrence of a so-called chromophoric group within the molecule. When such a group is known to be present the appearance of the corresponding absorption band can be expected. Even in the absence of definite combination between solvent and solute the precise location and intensity of this absorption band are not wholly predictable because of the effect of several variable factors such as the nature of the solvent, and, more particularly, the molecular environment of the chromophoric group. This point of view has been elaborated in Parts I and II (J., 1940, 1453; 1941, 815), in which chromophores containing two unsaturated linkages in conjugation have been considered, *i.e.*, (I) and (II). In this Part the absorption spectra of compounds containing the related chromophore (III) have been determined and discussed.

>C:C–C:C< (I.) >C:C–C:O (II.) >C:C–C:N– (III.)

In Part II (*loc. cit.*) light-absorption data on αβ-unsaturated ketones were presented and discussed in the light of Woodward's suggestion (*J. Amer. Chem. Soc.*, 1941, **63**, 1143; 1942, **64**, 76) that the location of the *K*-band in the absorption spectra of such compounds is controlled by the number of substituents on the chromophore, and in fact that the degree of substitution can be inferred from the location of the band. Thus if Cββ′:Cα·CR:O (IV) represents an αβ-unsaturated ketone where R is an alkyl group, and α, β, and β′ may be H (or any saturated hydrocarbon residue), we have Woodward's generalisation (*loc. cit.*) in its simplest form as follows :

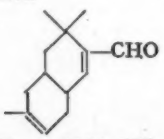
αβ-Unsaturated ketone.	Location of *K*-band, A.	αβ-Unsaturated ketone.	Location of *K*-band, A.	αβ-Unsaturated ketone.	Location of *K*-band, A.
Monosubstitution, α or β	2250 ± 50	Disubstitution, αβ or ββ	2350 ± 50	Trisubstitution, αββ	2470 ± 50

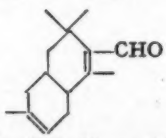
In Part II we had insufficient data on unsaturated aldehydes to justify their consideration, but there are now a sufficient number for a preliminary examination. In (IV), if we make R = H, we change from the unsaturated ketones to the unsaturated aldehydes, and since we have one alkyl group less here we might expect the substitution of H for alkyl to produce a displacement of the absorption band, due to the conjugated system, to shorter wave-lengths. In Table I are presented the absorption data on αβ-unsaturated aldehydes, and it will be seen that the maxima are, in fact, at shorter wave-lengths than for the corresponding ketones. Hence, to cover the majority of individual values in the unsaturated aldehyde series we must have a new set of empirically adjusted wave-lengths for λ max. in each of the three types of alkyl-substituted derivatives.

TABLE I.

Absorption spectra of αβ-unsaturated aldehydes and their semicarbazones in alcohol.

			K-Bands.						
			Aldehydes.		Semicarbazones.				
	R-Band.		C=C—C=O.		C=C—C=N.				Substitution of aldehyde.
Compound.	λ, max.	ε, max.	λ, max.	ε, max.	λ, max.	ε, max.	Δλ, A.	Δε.	
Acraldehyde	3278	12·6	2083 [1]	—	2645	19,000	—	—	—
Crotonaldehyde	3205	19·5	2170 [2]	15,650	2645	24,000	475	8,350	mono
Tiglinaldehyde	2900	11·3	2280	>5,000	2640	19,700	360	<10,000	di
β-Methylcrotonaldehyde [3]	—	—	2350	6,700	2730	33,460	380	26,760	di
α-Ethyl-Δ$^{\alpha}$-hexenaldehyde	3130	27	2285	10,670	2320	9,260	35	—	di
Citral [4]	3240	65	2380	13,500	2720	31,350	340	17,850	di
β-*cyclo*Citral [4]	3280	43	2445	8,300	2720	23,800	275	5,500	tri
*cyclo*Hexylideneacetaldehyde [5]	—	—	2320	17,400	2740	32,300	420	14,900	di
Phellandral:									
(*a*) *ex* water-fennel oil	—	—	2320	—	2650	24,500			
(*b*) *ex* phellandrene	—	—	2325	—	2650	24,200	307	5,730	di
(*c*) data by Cooke and Macbeth [6]	3125	417	2285	18,620	—	—			
α-Decylideneacetaldehyde [5]	—	—	2350	15,000	2730	32,400	380	17,400	di
β-Decylideneacetaldehyde [5]	—	—	2340	17,100	2740	31,000	400	13,900	di
Compound (V)	—	—	2350 [7]	14,000	2680	33,300	350	19,300	di
Compound (VI)	—	—	2400 [7]	8,000	2670	27,500	270	19,500	tri
Δ^{3}-2-Formylcholestene [8]	—	—	2350	12,600	—	—	—	—	di

(V.) 



(VI.)

[1] Luthy, *Z. physikal. Chem.*, 1923, **107**, 284. [2] Haüsser *et al.*, *Z. physikal. Chem.*, 1935, *B*, **29**, 371. [3] Barraclough, Thesis (Manchester University). [4] Burawoy, J., 1941, 20 (cf. also Bielecki and Henri, *Ber.*, 1914, **47**, 1690). [5] Dimroth, *Ber.*, 1938, **71**, 1333. [6] Cooke and Macbeth, J., 1938, 1408. [7] Batty, Heilbron, and Jones, J., 1939, 1556. [8] Plattner and Jampolsky, *Helv. Chim. Acta*, 1941, **24**, 1459.

The following set of values appears to fulfil the requirements for these aldehydes and is related to the above set for unsaturated ketones by being uniformly 50 A. lower:

αβ-Unsaturated aldehyde.	Location of *K*-band, A.	αβ-Unsaturated aldehyde.	Location of *K*-band, A.	αβ-Unsaturated aldehyde.	Location of *K*-band, A.
Monosubstitution, α or β	2200 ± 50	Disubstitution, αβ or ββ	2300 ± 50	Trisubstitution, αββ	2420 ± 50

Probably the simplest type of compound containing the group (III) is to be found in the semicarbazones of αβ-unsaturated ketones and aldehydes, and several workers have recorded the absorption spectra of isolated examples of such compounds (cf. Menschick *et al.*, *Annalen*, 1932, **495**, 225; Burawoy, J., 1941, 20). Figs. 1 and 2 show the absorption spectra of typical αβ-unsaturated ketones and their semicarbazones, the displacement of the maximum to longer wave-lengths, the disappearance of the band due to the carbonyl group, and a distinct increase in intensity of absorption being usually observed in passing from the carbonyl compound to its semicarbazone. Hence, the inference of the presence of the group (II) in a molecule from the occurrence of an absorption band situated between 2200 and 2500 A. and with ε of order 10,000, is very much strengthened by the observation that this band is displaced to longer wave-lengths with an increase in intensity in the semicarbazone.

These bathochromic and hyperchromic effects are evident from the data on ketones in Table II as well as from the figures. Table I shows the corresponding data on unsaturated aldehydes and their semicarbazones, and it is clear that the results with unsaturated ketones are closely paralleled by the data on the analogous aldehydes.

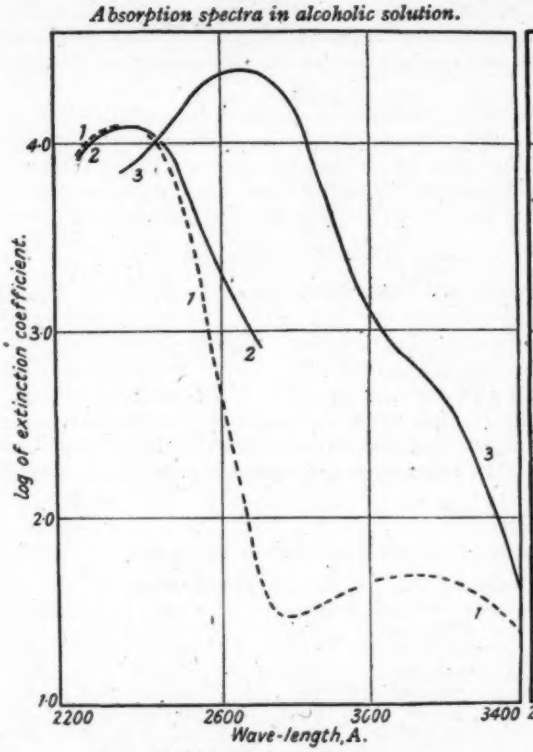
Pulegone appears to be exceptional among αβ-unsaturated ketones in that the location of the absorption band of its semicarbazone is scarcely displaced from that of the ketone. Menschick *et al.* (*loc. cit.*) give λ max. 2520 and 2530 A. for the ketone and the semicarbazone respectively, and we have confirmed these observations.

The anomaly is, of course, not so much in the small difference between these two values as in the low wave-length value for the location of the absorption band of the semicarbazone, since the wave-length of maximum absorption of pulegone itself is already unusually high because pulegone is a trisubstituted αβ-unsaturated ketone. On the other hand, the low wave-length value for the semicarbazone is hardly likely to be due to the presence of the unconjugated *iso*pulegonesemicarbazone, as this absorbs maximally near 2200 A. (Menschick *et al.*, *loc. cit.*).

Amongst the aldehydes, there is an almost exactly analogous case in α-ethyl-Δ$^{\alpha}$-hexenaldehyde where the semicarbazone gives an absorption band which is only slightly displaced to longer wave-lengths from that of the original carbonyl compound (35 A.) As in the case of pulegone, the intensity of absorption of the semicarbazone is much lower than usual (cf. Table II).

FIG. 1.

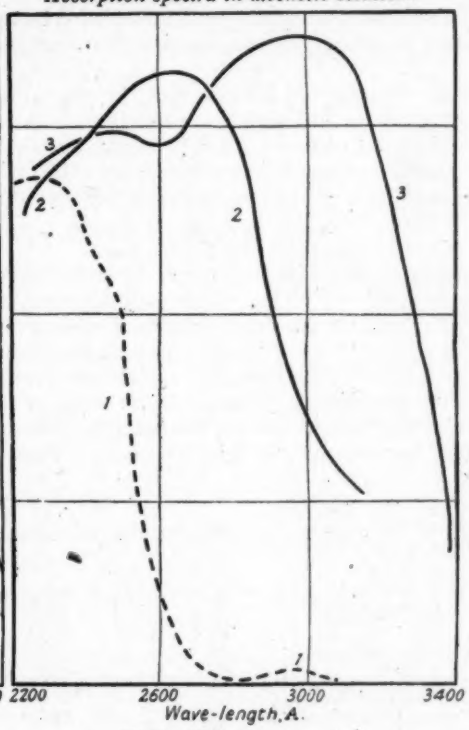
Absorption spectra in alcoholic solution.



1. 3-*Methyl*cyclo*hexen*-1-*one*.
2. ,, *oxime*.
3. ,, *semicarbazone*.

FIG. 2.

Absorption spectra in alcoholic solution.



1. *Tiglinaldehyde*.
2. ,, *semicarbazone*.
3. ,, *thiosemicarbazone*.

TABLE II.

Comparison of absorption spectra of αβ-unsaturated ketones and their semicarbazones.

	K-Bands only.					
	C=C–C=O.		C=C–C=N.			
Compound.	λ, max., A. †	ε, max.	λ, max., A.†	ε, max.	Δλ, A.	Δε.
CH_3·CO·CMe:CH_2	2180 [1]	8,300	2595	21,000	415	12,700
CH_3·$[CH_2]_2$·CH:CH·CO·CH_3	2280 [1]	10,600	2645	25,500	365	14,900
CH_3·CH_2·CO·CMe:CH_2	2200 [1]	7,880	2600	18,800	400	10,920
CH_3·CMe:CH·CO·CH_3	2350 [2]	14,000	2600 [3]	12,020	250	—
CH_3·CH:CMe·CO·CH_3	2295 [1]	11,090	2595	23,800	300	12,710
Piperitone	2355 [7]	17,780	2660	19,300	305	1,520
Carvone	2350 [9]	19,000	2660	21,200	310	2,140
1-Methyl*cyclo*hexen-3-one	2350 [1]	12,930	2655	25,700	305	12,770
2 : 3 : 4 : 5-Tetrahydroacetophenone	2335 [1]	9,660	2605	20,150	270	10,890
2 : 4-Dimethyl*cyclo*hexen-3-one	2365 [1]	6,840	2645	19,700	280	12,860
α-Ionone	2280 [4]	13,300	2635 [5]	31,600	355	18,300
Carvotanacetone [6]	2330	9,150	2680	24,900	350	15,750
*iso*Thujone [6]	2375	12,000	2670	24,800	295	12,800
Tetrahydropyrethrolone [8]	2320	12,200	2650	22,200	330	10,000
Dehydrojasmone [8]	2370	12,200	2665	20,400	295	8,200
$\Delta^{4\cdot7}$-Ergostadienone-3 [10]	2410	15,230	2670 *	36,830	320	21,600
Δ^1-Coprosten-3-one [11]	<2360	>5,840	2700 *	9,670	340	<3,830
Δ^4-Androstenedione-3 : 17 [13]	2380	16,500	2650 *	35,000	370	18,500
Δ^4-Cholesten-3-one	2400 [2]	16,220	2730	26,300	330	10,080
	2405 [12]	18,000	2705 [12]	26,000	300	8,000
Fucostadienone [12]	2400	17,000	2715	27,000	315	10,000
Stigmastadienone [12]	2410	17,000	2710	29,000	300	12,000
Sitostenone [12]	2410	17,000	2720	25,000	310	8,000

* Observed values in chloroform. † Values for ethyl-alcoholic solution.

[1] Evans and Gillam, J., 1941, 815. [2] Morton, J., 1926, 719. [3] Menschick, Page, and Bossert, *Annalen*, 1932, **495**, 225. [4] Gillam and West, *Nature*, 1941, **148**, 114. [5] Burawoy, J., 1941, 20. [6] Gillam and West, J., 1941, 811. [7] Gillam, Lynas-Gray, Penfold, and Simonsen, J., 1941, 60. [8] Gillam and West, J., 1942, 483. [9] Cooke and Macbeth, J., 1938, 1408. [10] Wetter and Dimroth, *Ber.*, 1937, **70**, 1665, 2033. [11] Inhoffen and Hueng-Minlon, *Ber.*, 1938, **71**, 1720. [12] Jones, Wilkinson, and Kerlogue, J., 1942, 391. [13] Butenandt and Peters, *Ber.*, 1938, **71**, 2690.

With these two exceptions, the absorption bands of the semicarbazones of some 33 αβ-unsaturated aldehydes and ketones all fall within the range 2670 ± 75 A., the intensities (ε) ranging from 10,000 to 35,000 with an average value near 26,000 (Tables I and II). It would therefore seem that the substituent effect observed in the unsaturated aldehydes and ketones disappears in the semicarbazones (see the similar case of the oximes, p. 570).

Although we accept as a useful fact the observation that semicarbazones have their main absorption band situated about 350 A. to longer wave-lengths than the chromophorically-similar oximes, no satisfactory explanation has yet been put forward. It would seem either that the molecular environment is sufficient to displace the absorption due to the chromophore (III) to longer wave-lengths in the semicarbazones, or that there might be an increase in the length of the conjugated system, possibly brought about by enolisation as follows:

$$CRR':CH\cdot CR:N\cdot NH\cdot CO\cdot NH_2 \longrightarrow CRR':CH\cdot CR:N\cdot N:C(OH)\cdot NH_2$$

We proceeded to test this hypothesis by examining the methylsemicarbazones derived from 2-methylsemicarbazide, $NH_2\cdot NMe\cdot CO\cdot NH_2$, where no such enolisation is possible.

The methylsemicarbazones of simple αβ-unsaturated aldehydes or ketones, however, could not be prepared. On the other hand, those of some aromatic aldehydes were easily obtained, and although it was desirable to avoid complication of the issue by the introduction of a phenyl chromophore, a comparison of the absorption spectra of the methylsemicarbazones with those of the corresponding unsubstituted semicarbazones might be expected to show the effect of the methyl group without the aromatic nature of part of the molecule influencing the results. Such was found to be the case (cf. Table III). It is thus clear that the only difference in the light

TABLE III.

Absorption spectra of semicarbazones and methylsemicarbazones (in alcohol).

	Semicarbazone.		Methylsemicarbazone.		
	λ, max., A.	ε, max.	λ, max., A.	ε, max.	Δλ, A.
Cinnamaldehyde	2295	9,580	2330	9,930	+35
	3100	40,200	3125	38,800	+25
o-Hydroxybenzaldehyde	2770	17,000	2805	16,250	+35
	3155	12,830	3215	13,200	+60
m-Hydroxybenzaldehyde	2840	20,800	2880	26,600	+40
p-Hydroxybenzaldehyde	2890	24,150	2910	24,100	+20
				Average increment =	36 A.

absorption of the two types of semicarbazones is a consistent displacement to longer wave-lengths in the case of the methyl derivatives. Both in direction and in size this displacement is typical of the normal substituent effect of a methyl group, and it is therefore evident that the chromophore responsible for the light absorption of semicarbazones in general cannot be the conjugated system of three double bonds produced by enolisation as suggested above. Burawoy's observation (J., 1939, 1177) that a hydroxy- or amino-group in conjugation with an ethylene linkage produces the equivalent of a conjugated system, provides an explanation, along the lines that the substituted amino-group in the semicarbazone in conjugation with the existing *K*-chromophore acts as though it were lengthening the conjugated system. This explanation is perfectly satisfactory in the case of the semicarbazones, but when a hydroxy-group is added to the system (III), as in the oximes, the bathochromic effect, if any, is very small (see below).

When considering semicarbazide derivatives of carbonyl compounds from the point of view of chromophoric make-up, the only other related compounds of interest here are the phenyl- and the thio-semicarbazones. The absorption spectra of some of the former have been examined (Burawoy, J., 1941, 20), but since they contain the NHPh– chromophore in addition to the simple group (III), their further discussion is out of place here. The thiosemicarbazones, on the other nand, are chromophorically simple derivatives of (III), and are of interest because they differ from ordinary semicarbazones only in having a sulphur atom replacing oxygen—*i.e.*, they constitute a new molecular environment for the chromophore under discussion without the complication of an additional chromophore. The absorption spectra of thiosemicarbazones have been little studied, and we record the data (Table IV) on a selection of these derivatives of αβ-unsaturated carbonyl compounds for comparison with their oxygen analogues.

Examination of the tabulated and graphical data (Table IV and Fig. 3) shows that, unlike the true semicarbazones, the sulphur analogues all show a second absorption band which is fairly constant in location and intensity. By comparison with the absorption of thiosemicarbazide, it is clear that this band (λ max. *ca.* 2450 A., ε of the order 10,000) is due to the thiosemicarbazide part of the molecule and not to the group (III) (cf. Ruzicka, Seidel, and Fermenich, *Helv. Chim. Acta*, 1941, **24**, 1434). The data in this table further show that the thiosemicarbazones of carbonyl compounds exhibit absorption bands due to the conjugated system situated some 600—700 A. further towards the visible spectrum than in the case of the original band due to C=C—C=O. There is also an increase in intensity which is even greater than that shown by ordinary semicarbazones.

The thiosemicarbazones are therefore very valuable derivatives of unsaturated carbonyl compounds from the point of view of the identification of the C=C—C=O group by absorption-spectra methods on account of the facts (*a*) that the absorption band is of very high intensity, (*b*) that it is displaced to a part of the spectrum which is especially suitable for accurate measurement, and, (*c*) that the band has moved so far up the spectrum

TABLE IV.

Absorption spectra of the thiosemicarbazones of αβ-unsaturated carbonyl compounds (in alcohol).

	Thiosemicarbazones.				Carbonyl compound.			
	Thiosemicarbazide band.		C=C–C=N Band.		*K*-Band.			
Carbonyl compound.	λ, max.	ε, max.	λ, max.	ε, max.	λ, max.	ε, max.	Δλ, A.	Δε.
Carvone	2450	8,400	3015	24,700	2353 [1]	19,000	662	5,700
Butylideneacetone	2460	10,150	3015	35,900	2280	10,600	735	25,300
Piperitone	2450	13,470	3020	32,200	2355	17,780	665	14,400
2 : 3 : 4 : 5-Tetrahydroacetophenone	2470	10,070	3010	37,000	2335	9,660	675	16,900
1-Methyl-Δ^1-*cyclo*hexen-3-one	2465	9,210	3025	30,350	2350	12,930	675	17,400
Irone [2]	2470	10,200	3010	32,000	2280	12,350	730	19,650
α-Ionone	2485	9,860	3025	36,500	2280	13,300	745	23,200
Tiglinaldehyde	2480	8,870	2995	29,950	2280	5,000	715	25,000
α-Ethyl-Δ^α-hexenaldehyde (Thiosemicarbazide) [3]	2450	9,200	3010	33,000	2285	10,670	725	22,330
	2410	13,800						

[1] Cooke and Macbeth, J., 1938, 1408. [2] Gillam and West, J., 1942, 483. [3] Ruzicka, Seidel, and Fermenich *loc. cit.*

that absorption due to many of the commoner absorbing impurities is left behind at shorter wave-lengths, thus giving a cleaner and more selective absorption band.

FIG. 3.

Absorption spectra in ethyl-alcoholic solution.

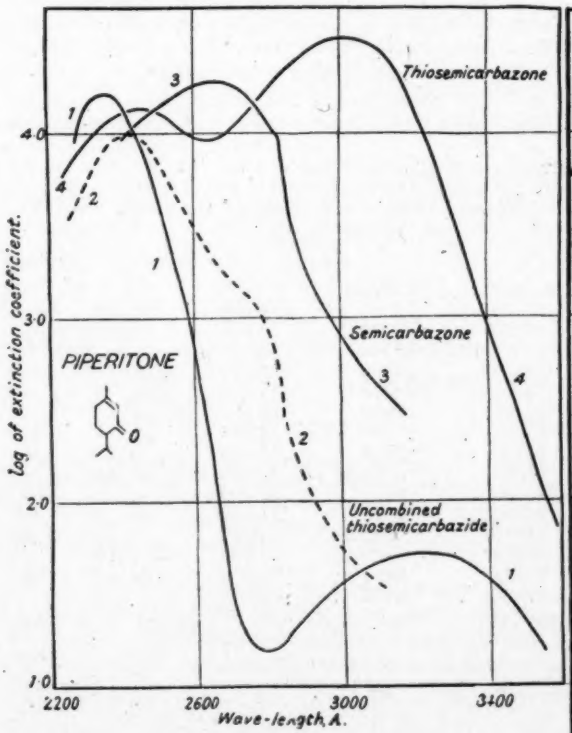
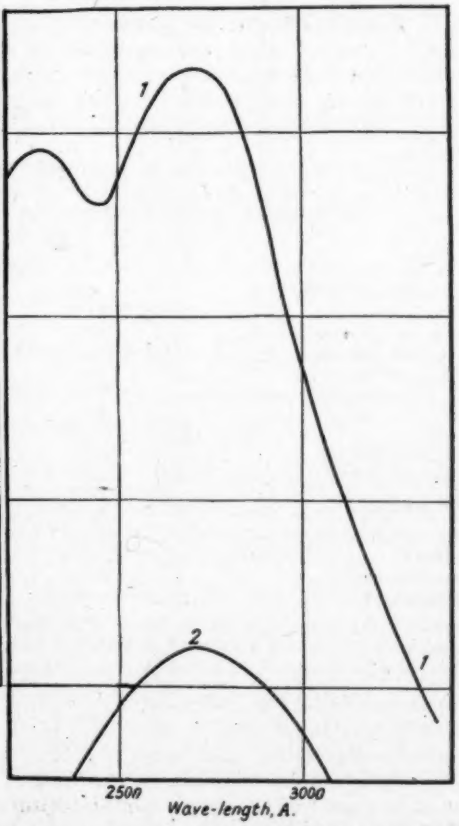


FIG. 4.

Comparison of the absorption spectrum of a saturated carbonyl compound (methyl ethyl ketone) (2) with that of its thiosemicarbazone (1).



In the thiosemicarbazones listed in Table IV the interesting point is the nearly constant location of the band at 3015 ± <20 A. It should be noted that no trisubstituted αβ-unsaturated compounds are represented, so the question whether trisubstitution would displace the band to longer wave-lengths or not must remain open.

We have seen that the simple semicarbazones of αβ-unsaturated carbonyl compounds absorb maximally near 2700 A., whilst those of the saturated analogues absorb at wave-lengths less than 2200 A., *i.e.*, almost outside the practicable range of the quartz spectrograph. In thiosemicarbazones the weighting effect of the sulphur atom apparently displaces the light absorption to longer wave-lengths. We have examined the

absorption spectra of the thiosemicarbazones of a number of typical *saturated* aldehydes and ketones and find that they exhibit two distinct absorption bands near 2300 and 2700 A. severally (Table V). From their intensities, we attribute the former to the thiosemicarbazide part of the molecule displaced by about 100 A. to shorter wave-lengths by the molecular environment (contrast the opposite effect in αβ-unsaturated carbonyl thiosemicarbazones). The 2700 A. band is presumably due to the pseudo-conjugated system —C=N—NHR (Burawoy,

TABLE V.

Absorption spectra of thiosemicarbazones of saturated carbonyl compounds (in alcohol).

Carbonyl compound.	Thiosemicarbazide band. λ, max., A.	ε, max.	Thiosemicarbazone band. λ, max., A.	ε, max.
Acetone	2285	7080	2710	21,200
Methyl ethyl ketone	2295	8130	2710	22,000
Methyl hexyl ketone	2300	7800	2715	23,200
*cyclo*Hexanone	2295	7900	2720	23,400
3-Methyl*cyclo*hexanone	2295	8400	2730	24,300
4-Methyl*cyclo*hexanone	2280	8270	2715	24,400
Acetaldehyde	2295	6800	2700	20,400
Propaldehyde	2290	6200	2700	20,580
Butaldehyde	2285	7600	2715	22,700

J., 1939, 1177) and has the intensity of a typical *K*-band. This observation gives us an additional spectroscopic method of detecting small amounts of *saturated* aldehydes or ketones *via* their thiosemicarbazones, since the absorption band of the latter is situated in an easily accessible region of the quartz ultra-violet, and, moreover, the absorption is some 500 times more intense than that of the original aldehyde or ketone (cf. Fig. 4 and Table V).

Another interesting type of compound derived from (III) is that represented by the oximes of αβ-unsaturated carbonyl compounds having the chromophoric group >C=C—C=N—OH. Data on typical oximes of unsaturated ketones and aldehydes are shown in Table VI and in Fig. 1. The light absorption of the oximes differs from that of the original carbonyl compounds in that it is a single absorption band only, the *R*-band (due to >C=O) having disappeared. On the other hand, the absorption of the oximes differs from that of the chromophorically similar semicarbazones in being situated at much shorter wave-lengths (displacement of the order 350 A.).

TABLE VI.

Absorption spectra of oximes of αβ-unsaturated ketones and aldehydes (in alcohol).

Carbonyl compound.	C=C—C=O Band. λ, max.	ε, max.	C=C—C=N. Band. λ, max.	ε, max.	Δλ, A.	Δε.
Crotonaldehyde	2170	15,650	2295	16,900	+125	+ 1250
Δ²-2-Formylcholestene [1]	2350	12,600	2330	20,000	− 20	+ 8000
1-Methyl*cyclo*penten-3-one [2]	—	—	2340	13,000	—	—
1-Methyl*cyclo*hexen-3-one	2350	12,930	2360	12,900	+ 10	− 30
2 : 3 : 4 : 5-Tetrahydroacetophenone	2335	9,660	2310	13,800	− 25	+ 4140
Carvone	2350	19,060	2360	16,050	+ 10	− 3010
Piperitone	2355	17,780	2360	>12,200	+ 5	−<5580
CH_2·CH:CMe·CO·CH_3	2295	11,090	2305	17,800	+ 10	+ 6710
CH_3·CMe:CH·CO·CH_3	2350	14,000	2365 [4]	12,600	+ 15	− 1400
Δ⁴-Cholesten-3-one	2405	18,000	2400	23,000	− 5	+ 5000
	2420	19,950	2420	17,600	± 0	− 2350
3-Acetoxy-Δ⁵-cholestene-7-one [3,6]	2340	14,010	2380	14,090	+ 40	+ 80
Sitostenone [5]	2410	17,000	2400	20,000	− 10	+ 3000
Stigmastadienone [5]	2410	17,000	2400	22,000	− 10	+ 5000
Fucostadienone [5]	2400	17,000	2405	23,000	+ 5	+ 6000

[1] Plattner and Jampolsky, *Helv. Chim. Acta*, 1941, **24**, 1459. [2] We are indebted to Professor A. R. Todd, F.R.S., for a specimen of this oxime. [3] Eckhardt, *Ber.*, 1938, **71**, 461. [4] Value in water, not alcohol. [5] Jones, Wilkinson, and Kerlogue, J., 1942, 391. [6] Solvent not given.

The oximes of αβ-unsaturated carbonyl compounds on which absorption data are presented here all absorb within the narrow range 2360 ± 65 A. with intensities (ε) ranging from 12,000 to 23,000. Except crotonaldoxime, all the compounds are derivatives of disubstituted αβ-unsaturated carbonyl compounds, and no trisubstituted members are included. There is thus very little information on the effect of substitution, but the location of the band of the single monosubstituted αβ-unsaturated aldehyde oxime (2295 A.) is so similar to that of the disubstituted carbonyl compounds that it seems probable that—as in the semicarbazones—the location of the oxime band is independent of the substitution of the parent carbonyl compound.

EXPERIMENTAL.

Determination of Absorption Spectra.—Except in the relatively few cases where the data were available in the literature, and to which references have been made, the absorption-spectra determinations were all carried out with a Hilger E_3 medium quartz spectrograph and Spekker photometer. Purified ethyl alcohol was used as solvent. Intensities of absorption are expressed in the usual form: Molecular extinction coefficient (ε) = $(\log I_0/I)/cl$, where I_0 and I are the intensities of the incident and the transmitted light, c the molar concentration, and l the thickness of the layer (in cm.).

Preparation of Compounds.—Unless otherwise stated, the aldehydes and ketones were either freshly distilled commercial products or those described in Part II (*loc. cit.*).

Phellandral. We are indebted to Dr. T. F. West for specimens of this compound obtained from different sources. In one case *d*-phellandral was isolated from water-fennel oil, converted into the semicarbazone, and regenerated. The resulting aldehyde (b. p. 77—78°/3 mm.) had $\alpha_D^{24°}$ 14·2°; $n_D^{21°}$ 1·4928. The second sample was obtained by oxidation of *l*-β-phellandrene, preparation of the semicarbazone (m. p. 203—204°), and regeneration. In both cases, although the semicarbazones were good products, owing to the small amounts available, the regenerated aldehydes were not perfectly pure as judged by the low intensity of their absorption bands (λ max. 2320 A., ε = 11,700; cf. λ max. 2285, ε = 18,620, quoted by Cooke and Macbeth, J., 1938, 1408).

Tiglinaldehyde. Several attempts were made to obtain this compound spectroscopically pure. Propaldehyde (50 ml.), prepared by oxidation of propyl alcohol (*Organic Syntheses*, XII, 64), was carefully fractionated and collected over the range 47—49°; it was condensed with acetaldehyde (39 ml.) by heating with 100 ml. of 27·7% sodium acetate solution in an autoclave at 100° for 24 hours (Lieben and Zeisel, *Monatsh.*, 1886, **7**, 54), and after three fractionations through a long column, the product had b. p. 116—118° (yield, 18·8 g.). This showed an unsymmetrical curve with ε max. of only 5,000 at 2280 A., indicating it to be still very impure. Variation in the proportion of the two aldehydes in the mixture before condensation gave no better result.

α-Ethyl-Δ$^{\alpha}$-hexenaldehyde. *n*-Butaldehyde (25 g.; prepared by oxidation of the alcohol), b. p. 73—74°, was shaken for several hours with 10% aqueous potassium hydroxide (5 ml.) in ether (15 ml.) (Weizmann and Garrard, J., 1920, **117**, 329). The product after three fractionations had b. p. 173—175° (yield, 6·5 g.).

Semicarbazones. These were prepared by the usual method from semicarbazide hydrochloride (1 mol.) and sodium acetate in aqueous alcohol, and recrystallised until the m. p.'s were constant and comparable with published values. The values obtained on our specimens were as follows: Methyl *iso*propenyl ketone, 174—176°; butylideneacetone, 116—117°; 3-methyl-Δ^{3}-penten-2-one, *ca.* 200° (decomp.); carvone, 152°; 2 : 3 : 4 : 5-tetrahydroacetophenone, 221·5°; piperitone, 222·5°; 1-methyl*cyclo*hexen-3-one, 197°; 2 : 4-dimethyl*cyclo*hexen-3-one, 203—205°; crotonaldehyde, 197·5°; tiglinaldehyde, 216°; α-ethyl-Δ$^{\alpha}$-hexenaldehyde, 130—130·5°.

2-Methylsemicarbazones. Nitrosomethylurea (*Organic Syntheses*, XV, 48) was reduced with zinc and acetic acid to give a solution of 2-methylsemicarbazide (Young and Oates, J., 1901, **79**, 659), from which the methylsemicarbazones were prepared (as described by Young and Oates) directly without isolation of the methylsemicarbazide. M. p.'s of the derivatives were as follows: Cinnamaldehyde, 154—155°; *o*-hydroxybenzaldehydemethylsemicarbazone, 171—172°; *m*-isomer, 182—184°; *p*-isomer softens 180—190°, clears at 230—240° (decomp.).

Thiosemicarbazones. The pure ketones and aldehydes were treated with thiosemicarbazide (1 mol.), prepared from hydrazine sulphate and potassium thiocyanate (Freund and Schander, *Ber.*, 1896, **29**, 2500) in aqueous-alcoholic solution. The precipitated derivatives were purified by crystallisation. The m. p.'s of the thiosemicarbazones (most of which are new) were: 1-Methyl*cyclo*hexen-3-one, 138—140°; tiglinaldehyde, 155°; α-ethyl-Δ$^{\alpha}$-hexenaldehyde, 160—162°; butylideneacetone, 150—151°; piperitone, 170—171°; carvone, 172—174° (decomp.); 2 : 3 : 4 : 5-tetrahydroacetophenone, 143—144°; acetone, 177°; *cyclo*hexanone, 156°; methyl ethyl ketone, 101—102°; 4-methyl*cyclo*hexanone, 161°; 3-methyl*cyclo*hexanone, 118—119°; methyl hexyl ketone, 69—70°; acetaldehyde, 140°; propaldehyde, 154—156°; *n*-butaldehyde, 108—109°.

Oximes. These were prepared from the carbonyl compound with hydroxylamine hydrochloride (1 mol.) and sodium acetate in aqueous alcohol and purified by recrystallisation. M. p.'s of the oximes of the following compounds were: Crotonaldehyde, 120·5°; 3-methyl-Δ^{3}-penten-2-one, 76·5°; 2 : 3 : 4 : 5-tetrahydroacetophenone, 97—98°; piperitone, 118°; carvone, 92·5°; 1-methyl*cyclo*hexen-3-one, 86—87°; Δ^{4}-cholesten-3-one, 152°.

UNIVERSITY OF MANCHESTER. [*Received, August* 31*st*, 1943.]

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151. *Experiments on the Synthesis of Purine Nucleosides. Part III. 4-Glycosidaminopyrimidines.*

By J. BADDILEY, B. LYTHGOE, and A. R. TODD.

Direct glycosidisation of 4-aminopyrimidines is complicated by the tendency of such compounds to behave as though they were derivatives of 4-iminodihydropyrimidine. Theoretical considerations suggested that glycosidisation of one of the amino-groups in derivatives of type (II) should be possible. This view has been justified experimentally and 6-*amino*-4-d-*xylosidamino*-2-*methylthiopyrimidine*, 6-*amino*-4-d-*mannosidamino*-2-*methylthiopyrimidine*, and 6-*amino*-4-d-*xylosidamino*-2-*methylpyrimidine* have been synthesised.

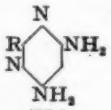
THE successful synthesis of purine nucleosides bearing a sugar residue at N_9 by the hypothetical route proposed in Part I (Baddiley, Lythgoe, McNeil, and Todd, this vol., p. 383) depends in the first place upon the availability of 5-amino-4-glycosidaminopyrimidines bearing appropriate substituents elsewhere in the molecule. Until now the only glycosidaminopyrimidines which have been synthesised are the 5-glucosidamino-compounds of Thannhauser and Dorfmüller (*Ber.*, 1914, **47**, 1304) obtained by direct condensation of 4 : 5-diaminopyrimidines with glucose in aqueous solution; under these conditions only the 5-amino-group reacts. It is evident from the ease of reaction in such cases that, for our purpose, either the 5-amino-group would have to be protected in some way or it would be necessary to glycosidise a 4-aminopyrimidine and subsequently to introduce an amino-group into position 5.

The glycosidisation of a 4-amino-group in a pyrimidine derivative, essential in either of the routes mentioned above, presents considerable difficulty and our early experiments in which we endeavoured to condense some readily available 4-amino-pyrimidines, *e.g.*, 4-amino-2-hydroxy-6-methylpyrimidine, 4-amino-5-aminomethyl-2-methylpyrimidine or their silver derivatives, with glucose or acetobromoglucose failed completely. These failures were not really surprising in view of the fact that, owing to the proximity of the annular nitrogen in position 3, such compounds in general behave as though they were derivatives of 4-iminodihydropyrimidine (I). We therefore next endeavoured, in a variety of uniformly unsuccessful experiments, to evade direct glycosidisation. Among these were several attempts to condense 1-aminoglucose (glucosimine) with 4-halogeno-

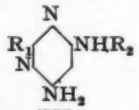
pyrimidines under various conditions; even with compounds such as 4-chloro-5-nitro-2-amino-6-methylpyrimidine and 2 : 4-dichloro-5-nitropyrimidine, in which the presence of a 5-nitro-group rendered the halogen in position 4 extremely reactive towards ammonia, no condensation could be effected. With the termination of these experiments it was decided to re-examine in more detail the problem of direct glycosidisation of substituted 4-aminopyrimidines.

Consideration of the tautomeric possibilities in substituted pyrimidines suggests that in a derivative of type (II) in which R represents H, alkyl or some substituent other than a group (*e.g.*, OH, SH, NH_2) capable of prototropic change, one double bond must occupy position 1 : 2 or 2 : 3 and hence one of the amino-groups at positions 4 and 6 should show, in considerable degree, the behaviour of a true amino-group. In this case one would expect direct glycosidisation of one amino-group in a compound of type (II) to be practicable. The validity of this argument appears to be borne out by our experimental results.

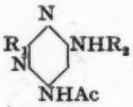
(I.)



(II.)



(III.)



(IV.)

As a model substance we selected in the first instance the readily accessible 4 : 6-diamino-2-methylthiopyrimidine (II; R = SMe). Although attempts to glucosidise by the action of acetobromoglucose on this substance or its silver derivative failed, application of the procedure used by Kuhn and Ströbele (*Ber.* 1937, **70**, 773) in preparing *N*-glycosides in the benzene series was successful. When refluxed in alcoholic solution with *d*-xylose or *d*-mannose in presence of ammonium chloride, (II; R = SMe) yielded crystalline glycosides which we regard as 6-*amino*-4-d-*xylosidamino*-2-*methylthiopyrimidine* (III; R_1 = SMe, $R_2 = C_5H_9O_4$) and 6-*amino*-4-d-*mannosidamino*-2-*methylthiopyrimidine* (III; R_1 = SMe, $R_2 = C_6H_{11}O_5$) respectively. Under similar conditions *d*-xylose and 4 : 6-diamino-2-methylpyrimidine (II; R = Me) gave 6-*amino*-4-d-*xylosidamino*-2-*methylpyrimidine* (III; R_1 = Me, $R_2 = C_5H_9O_4$).

Of the glycosidic nature of these products there can be no doubt; they are readily hydrolysed by dilute acids to the original constituents, and hence there can have been no Amadori rearrangement (Kuhn and Dansi, *Ber.*, 1936, **69**, 1745; Kuhn and Weygand, *ibid.*, 1937, **70**, 769) during their preparation. The possibility that they are Schiff bases is ruled out by the ready conversion of (III; R_1 = SMe, $R_2 = C_5H_9O_4$) into a *tetra-acetyl* derivative [IV; R_1 = SMe, $R_2 = C_5H_6O(OAc)_3$] in which one acetyl residue is attached to the 6-amino-group. Hydrolysis of this acetyl derivative with sodium methoxide in methanol gave 6-*acetamido*-4-d-*xylosidamino*-2-*methylthiopyrimidine* (IV; R_1 = SMe, $R_2 = C_5H_9O_4$), which underwent further hydrolysis with hot dilute acid to *d*-xylose and 4-*amino*-6-*acetamido*-2-*methylthiopyrimidine* (IV; R_1 = SMe, R_2 = H) identical with the product obtained on acetylation of (II; R = SMe) with acetic anhydride in pyridine solution at room temperature. In a similar manner (III; R_1 = SMe, $R_2 = C_6H_{11}O_5$) gave on acetylation a *penta-acetyl* derivative [IV; R_1 = SMe, $R_2 = C_6H_7O(OAc)_4$], hydrolysed successively to 6-*acetamido*-4-d-*mannosidamino*-2-*methylthiopyrimidine* (IV; R_1 = SMe, $R_2 = C_6H_{11}O_5$) and to 4-amino-6-acetamido-2-methylthiopyrimidine and *d*-mannose. The ready hydrolysis of the new glycosides with dilute acids is evidence for the location of the sugar residue, since pyrimidine derivatives in which sugar is linked to a nuclear nitrogen are known to be resistant to acid hydrolysis. In the experiments of Kuhn and Ströbele (*loc. cit.*) it was found that *N*-pentosides prepared by their method had a furanose structure. Whether the 4-glycosidamino-compounds here described have a furanose or a pyranose structure is not yet established, but experiments to this end are in progress.

In connection with the reasons, outlined above, which led to the selection of 4 : 6-diaminopyrimidines of type (II) for glycosidisation, it is interesting to note that we have so far failed to obtain any trace of glycoside formation under similar conditions with 4-amino-2 : 6-dimethylpyrimidine (cyanmethine), 4 : 6-diamino-2-thiolpyrimidine, 4 : 6-diamino-5-benzeneazopyrimidine, and 4 : 6-diamino-5-thioformamidopyrimidine. In the case of the first two compounds amidine-type tautomerism involving the amino-groups is unchecked. Failure to glycosidise 4 : 6-diamino-5-benzeneazopyrimidine might be explained in several ways; the benzeneazo-group may introduce a steric factor or new possibilities of tautomerism or the insolubility of the substance in alcohol might of itself be sufficient explanation. The failure to glycosidise 4 : 6-diamino-5-thioformamidopyrimidine was unexpected, but it is probably connected with the extremely low solubility of the compound in alcohol.

Experimental.

The activated aluminium oxide used in these experiments was prepared by heating "Alumina hydrate" (British Aluminium Co., Ltd.) from 20° to 360° with stirring during 5 hours.

6-*Amino*-4-d-*xylosidamino*-2-*methylthiopyrimidine*.—*d*-Xylose (4 g.), 4 : 6-diamino-2-methylthiopyrimidine (12 g.), and ammonium chloride (0·75 g.) were refluxed with ethyl alcohol (100 c.c.; dried over magnesium ethoxide) for 4 hours, and the cooled solution passed through a column of activated aluminium oxide (500 g.). The column was washed with alcohol (2·5 l.) and the filtrate and washings were united and evaporated, giving unchanged 4 : 6-diamino-2-methylthiopyrimidine (8 g.). Elution of the column with ice-cold water (2·5 l.) or with a pyridine–water–methanol mixture (1 : 1 : 2; 2·5 l.) and evaporation of the eluate in a vacuum at 20° gave a pale amber gum (dry weight 8 g.). This was freed from inorganic matter by dissolution in absolute alcohol; the solution was evaporated in a vacuum to 40 c.c., and ethyl acetate (40 c.c.) added. After 5 days the crystalline crust of 6-*amino*-4-d-*xylosidamino*-2-*methylthiopyrimidine* was collected, m. p. 190—192° (decomp.). Yield, 0·6 g. (Found: C, 41·5; H, 5·6; S, 11·7. $C_{10}H_{16}O_4N_4S$ requires C, 41·7; H, 5·5; S, 11·1%). Evidence is presented below showing that the gummy reaction product contains further considerable

quantities of the same material, but its separation in crystalline condition is attended with great difficulty. The substance is moderately readily soluble in water and pyridine, sparingly soluble in alcohol, and insoluble in other common organic solvents. Fehling's solution is not reduced below 60°; at higher temperatures reduction takes place slowly.

Hydrolysis. The xyloside (0·2 g.) was refluxed with N/10-hydrochloric acid (5 c.c.) for ½ hour, and the solution cooled, treated with N/10-sodium hydroxide (5 c.c.), and concentrated to 5 c.c. in a vacuum. Addition of a hot concentrated solution of picric acid (0·2 g.) and cooling gave 4 : 6-*diamino*-2-*methylthiopyrimidine picrate*, needles, m. p. 212° (decomp.), undepressed on admixture with a specimen prepared from the authentic diamine. Yield, 0·2 g. (Found : C, 34·2; H, 2·5. $C_6H_8N_4S,C_6H_3O_7N_3$ requires C, 34·3; H, 2·9%).

A second portion of xyloside was hydrolysed in similar fashion, and the solution heated for 1 hour with phenylhydrazine in acetic acid. On cooling, *d*-xylosazone separated, m. p. 159° alone or mixed with an authentic specimen.

6-*Acetamido*-4-*triacetyl*-d-*xylosidamino*-2-*methylthiopyrimidine*.—(a) *From crystalline* 6-*amino*-4-d-*xylosidamino*-2-*methylthiopyrimidine*. The crystalline xyloside (0·1 g.) in dry pyridine (10 c.c.) was treated at room temperature with acetic anhydride (1 c.c.) and acetyl chloride (0·1 c.c.), and the solution heated on the steam-bath for 1 hour. After cooling, ethyl alcohol (5 c.c.) was added to destroy the excess of acetic anhydride, the solution kept for 1 hour, and solvents removed in a vacuum. The residue, freed from pyridine by evaporation in a vacuum with ethyl alcohol, was crystallised from ethyl alcohol, giving 6-*acetamido*-4-*triacetyl*-d-*xylosidamino*-2-*methylthiopyrimidine* in needles (30 mg.), m. p. 226° (decomp.), $[\alpha]_D^{18°}$ + 57° (pyridine, c = 5·1%) (Found : C, 47·3; H, 5·3; N, 12·5. $C_{18}H_{24}O_8N_4S$ requires C, 47·3; H, 5·3; N, 12·3%).

(b) *From the gummy eluate material* (Experiment by Mr. A. Topham). A portion (5 g.) of this material, from which the crystalline xyloside had been separated, acetylated in pyridine (40 c.c.) with acetic anhydride (12 c.c.) and acetyl chloride as described for the crystalline xyloside, gave the same tetra-acetyl compound (2·25 g.), m. p. 226°, undepressed in admixture with a specimen prepared as in (a) above. This shows that there is present in the eluate gum considerably more 6-amino-4-*d*-xylosidamino-2-methylthiopyrimidine than can be readily separated in crystalline form.

6-*Acetamido*-4-d-*xylosidamino*-2-*methylthiopyrimidine*.—To the above tetra-acetyl compound (6 g.) in dry chloroform (60 c.c.), methyl-alcoholic sodium methoxide (0·7 g. of sodium in 100 c.c. of methyl alcohol) was added at room temperature. After 15 minutes water (400 c.c.) was added, the mixture well shaken, and the aqueous layer removed, neutralised by addition of sulphuric acid, and concentrated in a vacuum to 100 c.c.. The 6-*acetamido*-4-d-*xylosidamino*-2-*methylthiopyrimidine* which separated crystallised from water in needles, m. p. 95—100°, containing varying quantities of water of crystallisation, or from ethyl alcohol in rosettes (also hydrated), m. p. 192—193°. Yield, 2·5 g. (Found in material dried over phosphoric oxide at 100°/0·1 mm. : C, 43·6; H, 5·5; N, 16·7. $C_{12}H_{18}O_5N_4S$ requires C, 43·6; H, 5·45; N, 17·0%). The anhydrous substance had $[\alpha]_D^{20°}$ + 23° (pyridine, c = 2·1%).

Hydrolysis. The above xyloside (0·2 g.) in N/10-sulphuric acid (10 c.c.) was heated under reflux at 95° for ½ hour. The solution on cooling and neutralisation with N-sodium hydroxide (1 c.c.) gave 4-amino-6-acetamido-2-methylthiopyrimidine, which formed colourless crystals (50 mg.) from hot water, m. p. 225—226°, undepressed in admixture with material prepared as described below.

Acetylation of 4 : 6-*Diamino*-2-*methylthiopyrimidine*.—(a) 4 : 6-Diamino-2-methylthiopyrimidine (1 g.) in pyridine (10 c.c.) was kept overnight at room temperature with acetic anhydride (10 c.c.). Removal of solvents and crystallisation of the residue from water gave the acetyl derivative, m. p. 225—226°.

(b) 4 : 6-Diamino-2-methylthiopyrimidine (0·5 g.) in ethyl acetate (5 c.c.) was refluxed for 1 hour with acetyl chloride (1·5 c.c.). Removal of solvents and crystallisation of the residue from alcohol gave the *hydrochloride*, m. p. 213—214° (Found : C, 33·8; H, 5·2; N, 22·7. $C_7H_{10}ON_4S,HCl,H_2O$ requires C, 33·5; H, 5·2; N, 22·3%). Yield, 90%. Dissolution in water and addition of alkali gave the free base, m. p. 225—226°, undepressed in admixture with material prepared by the routes described above.

6-*Amino*-4-d-*mannosidamino*-2-*methylthiopyrimidine*.—*d*-Mannose (8 g.), 4 : 6-diamino-2-methylthiopyrimidine (24 g.), and ammonium chloride (0·75 g.) were refluxed together in dry alcohol (250 c.c.) for 3½ hours, and the solution cooled. The separated solid was washed thoroughly with alcohol and crystallised from hot water. 6-*Amino*-4-d-*mannosidamino*-2-*methylthiopyrimidine* separated in tiny hydrated needles (12 g.), m. p. 213—214° (decomp.). On drying, part of the water of crystallisation was readily removed, but the remainder appeared to cling tenaciously (Found in material dried for 1 hour over phosphoric oxide at 100°/0·1 mm. : C, 38·7; H, 5·9; N, 16·7. $C_{11}H_{18}O_5N_4S,1·5H_2O$ requires C, 38·3; H, 6·1; N, 16·2%).

Hydrolysis. The above mannoside (1 g.) and N/10-sulphuric acid (70 c.c.) were heated under reflux at 95° for 40 minutes, and the solution cooled, neutralised with N-sodium hydroxide (7 c.c.), and evaporated to dryness in a vacuum. The residue was extracted with hot alcohol (100 c.c.), and the extract passed through a column of activated aluminium oxide (50 g.), which was then washed with alcohol (150 c.c.). Filtrate and washings, united and evaporated, gave 4 : 6-diamino-2-methylthiopyrimidine (0·3 g.), m. p. 186°, undepressed on admixture with an authentic specimen. The column was eluted with cold water (250 c.c.), and the eluate united with the residue from the alcohol extraction and evaporated to 7 c.c., a little inorganic material separating being removed by filtration. Addition of anhydrous sodium acetate (1 g.) and phenylhydrazine hydrochloride (0·5 g.) to the solution gave *d*-mannose phenylhydrazone, separating from dilute alcohol in colourless crystals (0·5 g.), m. p. 189—191° (Fischer, *Ber.*, 1887, **20**, 821, gives m. p. 188—190°).

6-*Acetamido*-4-*tetra-acetyl*-d-*mannosidamino*-2-*methylthiopyrimidine*.—The above mannoside (1 g.) in dry pyridine (15 c.c.) was heated on the steam-bath for 1 hour with acetic anhydride (4 c.c.) and acetyl chloride (0·2 c.c.). After decomposition with ethyl alcohol and removal of solvents in the usual manner the residue was crystallised from ethyl alcohol, giving 6-*acetamido*-4-*tetra-acetyl*-d-*mannosidamino*-2-*methylthiopyrimidine* in needles, m. p. *ca.* 140—150°. Repeated crystallisation from alcohol, benzene and acetone–chloroform–petroleum gave crystals with the same characteristics. Yield, 1 g. (Found in material dried over calcium chloride at room temperature : C, 43·2; H, 5·4; N, 9·7; loss at 100°/0·1 mm., 9·3. $C_{21}H_{28}O_{10}N_4S,3H_2O$ requires C, 43·3; H, 5·8; N, 9·6; H_2O, 9·3%). The anhydrous substance had $[\alpha]_D^{20°}$ − 100° (pyridine, c = 16·0%).

6-*Acetamido*-4-d-*mannosidamino*-2-*methylthiopyrimidine*.—The above penta-acetyl derivative (7 g.) in dry chloroform (35 c.c.) was mixed with methyl-alcoholic sodium methoxide (1 g. of sodium in 50 c.c. of alcohol). After 15 minutes the resulting gel was shaken with ice-water (300 c.c.), and the aqueous layer separated, neutralised with acetic acid, and evaporated to 20 c.c. The 6-*acetamido*-4-d-*mannosidamino*-2-*methylthiopyrimidine* was collected and recrystallised from hot water, forming colourless needles (1·7 g.), m. p. 242—243° (decomp.), $[\alpha]_D^{20°}$ − 55° (pyridine, c = 0·7%) (Found : C, 43·4; H, 5·5; N, 15·3. $C_{13}H_{20}O_5N_4S$ requires C, 43·3; H, 5·6; N, 15·6%).

Hydrolysis. The above compound (0·2 g.) was heated with N/10-sulphuric acid (10 c.c.) under reflux at 95° for 45 minutes. The solution, cooled, neutralised with N-sodium hydroxide (1 c.c.), and evaporated to half its volume, gave 6-acetamido-4-amino-2-methylthiopyrimidine (50 mg.), m. p. 225—226°, undepressed in admixture with an authentic specimen.

6-*Amino*-4-d-*xylosidamino*-2-*methylpyrimidine*.—4 : 6-Diamino-2-methylpyrimidine (36 g.) (Baddiley, Lythgoe, McNeil, and Todd, *loc. cit.*), *d*-xylose (10 g.), anhydrous ethyl alcohol (500 c.c.), and ethyl-alcoholic hydrogen chloride

(4 c.c., saturated at 20°) were refluxed together for 72 hours in a flask fitted with a Fenske column and a reflux ratio head, water formed in the reaction being removed periodically as the ternary mixture by addition of a mixture of benzene and ethyl alcohol (2 : 1; total, 500 c.c.). The cooled solution was passed through a column of activated aluminium oxide (700 g.), which was then washed with ethyl alcohol (2 l.). Evaporation of filtrate and washings gave unchanged 4 : 6-diamino-2-methylpyrimidine (25 g.). Elution of the column with water (6 l.) and evaporation of the eluate in a vacuum below 30° to small volume gave crystalline 6-*amino*-4-d-*xylosidamino*-2-*methylpyrimidine*, m. p. 219° (decomp.), $[\alpha]_D^{20°}$ + 158° (water; c = 0·095%). Yield, 65% (Found: C, 46·6; H, 6·1; N, 21·4. $C_{10}H_{16}O_4N_4$ requires C, 46·9; H, 6·2; N, 21·8%).

Hydrolysis. (*a*) The above xyloside (0·3 g.) was refluxed with N/10-hydrochloric acid (25 c.c.) for 20 minutes, and the solution cooled, neutralised to Congo-red by addition of sodium hydroxide, and evaporated to dryness in a vacuum. The residue was extracted thrice with boiling alcohol, and the combined extracts (15 c.c.) passed through a column of activated aluminium oxide (15 g.), which was then washed with alcohol (70 c.c.). Evaporation of filtrate and washings gave 4 : 6-diamino-2-methylpyrimidine, m. p. 294°, undepressed in admixture with an authentic specimen.

(*b*) The xyloside (0·3 g.) was hydrolysed as above, and the neutralised solution concentrated to 12 c.c., treated with a solution of phenylhydrazine (0·3 g.) in acetic acid (2 c.c. of 40%), and heated at 100° for 1 hour. On cooling, *d*-xylosazone separated; it formed needles from aqueous alcohol, m. p. 158°, undepressed in admixture with authentic *d*-xylosazone (m. p. 158°).

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152. *Experiments on the Synthesis of Purine Nucleosides. Part IV. 4 : 6-Diaminopyrimidine. A New Synthesis of Pyrimidine Derivatives.*

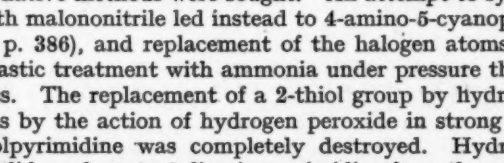
By G. W. KENNER, B. LYTHGOE, A. R. TODD, and A. TOPHAM.

The preparation of 4 : 6-diaminopyrimidine, required as starting material for nucleoside synthesis, by the method of Büttner (*Ber.*, 1903, **36**, 2227), by amination of 4 : 6-*dichloropyrimidine* or from 4 : 6-diamino-2-thiolpyrimidine, is unsatisfactory. A convenient method has been found in the condensation of malondiamidine with ethyl formate. This route, also applied to the preparation of 4 : 6-diamino-2-methylpyrimidine, represents a new method of synthesising the pyrimidine nucleus.

IN applying the experience of model experiments described in previous papers of this series (this vol., pp. 383, 386, preceding paper) to the synthesis of adenine-9-glycosides (*e.g.*, adenosine), the obvious starting material is 4 : 6-diaminopyrimidine. The alternative of starting with a 2-substituted 4 : 6-diaminopyrimidine and replacing the 2-substituent in the final nucleoside by hydrogen is complicated by the instability of the nucleosides under acid conditions. Although this alternative has not been neglected in our investigations, the route starting from 4 : 6-diaminopyrimidine seemed the more attractive for initial study.

4 : 6-Diaminopyrimidine has been described by Büttner (*Ber.*, 1903, **36**, 2227), who prepared it by an involved series of reactions from barbituric acid; the analytical data were rather unsatisfactory and the yield was recorded as " very small." We repeated Büttner's work with slight modifications in detail and confirmed the production of 4 : 6-diaminopyrimidine, but the overall yield was so low as to make the method useless for preparative purposes, and alternative methods were sought. An attempt to synthesise the substance directly by condensing formamidine with malononitrile led instead to 4-amino-5-cyanopyrimidine (Part II; Baddiley, Lythgoe, and Todd, this vol., p. 386), and replacement of the halogen atoms in 4 : 6-*dichloropyrimidine* by amino-groups required such drastic treatment with ammonia under pressure that the pyrimidine nucleus was largely destroyed in the process. The replacement of a 2-thiol group by hydrogen can frequently be accomplished in the pyrimidine series by the action of hydrogen peroxide in strong acid solution, but under these conditions 4 : 6-diamino-2-thiolpyrimidine was completely destroyed. Hydrogen peroxide in presence of acetic acid and sodium acetate did produce 4 : 6-diaminopyrimidine from the corresponding 2-thiol compound, but again the yield was extremely low.

The comparative failure of these experiments led us to examine the possibility of direct synthesis by new methods. It is known that diamino-1 : 3 : 5-triazines may be synthesised by the condensation of biguanide with esters (Rackmann, *Annalen*, 1910, **376**, 180). By analogy it seemed possible that ethyl formate might condense with malondiamidine (I) to give 4 : 6-diaminopyrimidine as indicated below:



(I.)

This proved to be the case. The hitherto undescribed malondiamidine (conveniently isolated as its *dihydrochloride*), prepared from malononitrile *via malondi-iminoether*, reacted readily with ethyl formate, giving 4 : 6-diaminopyrimidine in moderately good yield. In the same way ethyl acetate and malondiamidine yielded 4 : 6-diamino-2-methylpyrimidine. Apart from making 4 : 6-diaminopyrimidine readily accessible, this route is attractive as a potential general method for the synthesis of 2-substituted 4 : 6-diaminopyrimidines, and an investigation of it from this standpoint will be reported in due course.

Experimental.

4 : 6-*Dichloropyrimidine.*—4 : 6-Dihydroxypyrimidine (22 g.) (Kenner, Lythgoe, Todd, and Topham, this vol., p. 389) was refluxed with phosphoryl chloride (300 g.) and dimethylaniline (12 c.c.) until hydrogen chloride evolution ceased (*ca.* 3 hours). Unchanged phosphoryl chloride was removed in a vacuum, the residue poured on ice and extracted with ether, and the extract washed with sodium carbonate solution, dried, and evaporated. The *product* (15 g.) could be further purified by distillation (b. p. 176°) or by recrystallisation from light petroleum; it then had m. p. 67·5° (Found : C, 31·7; H, 1·5; Cl, 47·7. $C_4H_2N_2Cl_2$ requires C, 32·2; H, 1·4; Cl, 47·7%).

4 : 6-*Diaminopyrimidine from* 4 : 6-*Dichloropyrimidine.*—The above dichloro-compound (30 g.) was heated in an autoclave with alcoholic ammonia (750 c.c., saturated at 0°) at 170° during 8 hours. After evaporation the resulting mixture was extracted with *n*-butanol, and the extract agitated with two successive portions (250 g.) of aluminium oxide (activated by heating to 360°) and finally evaporated. The residue (11 g.), recrystallised from alcohol, gave yellowish crystals (3 g.), m. p. 260°; this material, after sublimation in a vacuum and a further recrystallisation from ethyl acetate–alcohol, gave colourless needles of 4 : 6-diaminopyrimidine, m. p. 267°, undepressed in admixture with material obtained by other methods described below (Found : C, 43·9; H, 5·5; N, 50·2. Calc. for $C_4H_6N_4$: C, 43·7; H, 5·5; N, 50·9%). The amination of the dichloro-compound was attempted under a variety of conditions both alcoholic ammonia and liquid ammonia being used, but no better results were obtained. When the temperature was raised above 200°, the sole product isolated was a liquid, b. p. 200°, apparently formoethylamide.

4 : 6-*Diaminopyrimidine from* 4 : 6-*Diamino-2-thiolpyrimidine.*—To sodium acetate (9·5 g.), dissolved in water (40 c.c.), a solution of 4 : 6-diamino-2-thiolpyrimidine (5 g.) in hot acetic acid (80 c.c.) was added. After cooling to 30°, hydrogen peroxide (17 c.c. of 100 vol., diluted to 40 c.c. with water) was added; the temperature rose slowly and was prevented by external cooling from exceeding 50°. After 1 hour the slightly turbid solution was evaporated in a vacuum, the residue taken up in water, and excess of aqueous picric acid added. The *picrate* was collected, dissolved in hot dilute sulphuric acid, and the solution cooled and extracted with nitrobenzene and then ether. The aqueous layer was neutralised with barium carbonate, filtered, and evaporated to dryness in a vacuum. Sublimation of the residue at 160°/10^{-2} mm. gave a small amount of 4 : 6-diaminopyrimidine in colourless needles, m. p. 269—271° (Found : C, 43·4; H, 5·4; N, 50·3%). A similar experiment, lead acetate being used in place of sodium acetate, failed to yield any of the desired product.

4 : 6-*Diaminopyrimidine from* 6-*Iodo-4-aminopyrimidine* (cf. Büttner, *loc. cit.*).—6-Iodo-4-aminopyrimidine (1·3 g.) was heated with alcoholic ammonia (1 g. of ammonia in 8 c.c. of alcohol) in a sealed tube at 180—200° during 2 hours; after cooling, the filtered solution was evaporated. The residual oil set on scratching to a pasty mass, which was extracted with ethyl acetate. A considerable proportion went into solution, but no product of definite m. p. could be obtained from the extract. The unextracted material could not be purified by recrystallisation, but sublimation in a vacuum at 160° gave colourless needles (0·22 g.), m. p. 268°, undepressed in admixture with 4 : 6-diaminopyrimidine prepared from 4 : 6-diamino-2-thiolpyrimidine.

Malondi-iminoether Dihydrochloride.—A rapid stream of dry hydrogen chloride was passed into a well-cooled and stirred solution of malononitrile (7·9 g.) in absolute alcohol (13·9 c.c.) and dry ether (150 c.c.) until saturated. Stirring was continued for 2 hours, by which time separation of the *iminoether dihydrochloride* was complete; it was collected (27 g.), washed thoroughly with dry ether, and dried in a desiccator over potassium hydroxide (Found by Volhard titration : *M*, 236. $C_7H_{14}O_2N_2,2HCl$ has *M*, 231). This preparation can be conveniently carried out on 200 g. portions of malononitrile, the yield being nearly theoretical. A similar method for preparing this compound is given in Houben–Weyl, "Die Methoden der Organischen Chemie," 2nd Edn., IV, 312, reference being made to a private communication from Houben and Blaise. No analysis of the substance is given, nor have we found any other mention of it in the literature.

Malondiamidine Dihydrochloride.—The above iminoether dihydrochloride (25 g.) was added to cold alcoholic ammonia (100 c.c. of alcohol saturated at 0° and diluted with 100 c.c. of alcohol), and the mixture kept for 2 days. The *malondiamidine dihydrochloride* which separated (11 g.) was collected, washed with ether, and dried (Found by Volhard titration : *M*, 172. $C_3H_8N_4,2HCl$ has *M*, 172). A further amount of the same substance could be obtained by concentrating the mother-liquors. By treatment of an absolute alcoholic solution of the dihydrochloride with 2 equivs. of sodium ethoxide, filtration and evaporation, malondiamidine was obtained as a deliquescent crystalline mass. For the preparation of large quantities of the dihydrochloride, 650 g. of the iminoether dihydrochloride, kept for 2 days with 3 l. of alcoholic ammonia (saturated at 0°), gave in a yield of 80% a product sufficiently pure (90%) for most purposes.

4 : 6-*Diaminopyrimidine.*—An ice-cold solution of sodium (38 g.) in dry methanol (500 c.c.) was added to malondiamidine dihydrochloride (140 g.), precipitated sodium chloride removed, and the solution evaporated at 30° in a vacuum. After the residual amidine had been washed with dry benzene (150 c.c.) by decantation, ethyl formate (500 c.c.) was added. After the initial violent reaction subsided, the mixture was refluxed for several hours and then evaporated. The crude product (88 g.) was not readily purified by simple recrystallisation, and sublimation, effective on a small scale, was inconvenient; after various trials the following procedure was adopted. The crude material (1 part), dissolved in alcohol, was allowed to flow through a column of aluminium oxide (20 parts, activated by heating to 360°), the column being well washed with alcohol; the combined filtrate and washings were evaporated, and the residue recrystallised from alcohol, giving colourless needles (39 g.), m. p. 267—268°, undepressed in admixture with 4 : 6-diaminopyrimidine prepared by other routes (Found : N, 51·2. Calc. for $C_4H_6N_4$: N, 50·9%). The substitution of ethyl orthoformate for ethyl formate in the above reaction gave much lower yields, and formamidine or a mixture of formic acid and sodium formate, heated with malondiamidine, gave at most only traces of the desired product.

4 : 6-*Diamino-2-methylpyrimidine.*—In the course of some other experiments ethyl acetate (500 c.c.) was added to malondiamidine (from 250 g. of crude dihydrochloride). There was immediate reaction, and the solid which separated was collected and extracted (Soxhlet) with alcohol. The extract on concentration yielded 4 : 6-diamino-2-methylpyrimidine; recrystallised from water, it had m. p. 296—297°, undepressed in admixture with an authentic specimen, m. p. 295° (Part I; Baddiley, Lythgoe, McNeil, and Todd, this vol., p. 383). The total yield (*ca.* 13 g.) was low, but subsequent experiments, carried out by the procedure used above in the analogous case of 4 : 6-diaminopyrimidine, have shown that yields of 40% are readily obtainable.

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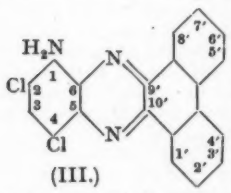
153. *Derivatives of* 1 : 2 : 4 : 5-*Tetrachlorobenzene. Part III. The Amination of* 2 : 3 : 5 : 6-*Tetrachloro-nitrobenzene and* -4-*nitroaniline.*

By A. T. Peters, F. M. Rowe, and D. M. Stead.

The nitro-group and, to a less extent, both chlorine atoms ortho to it in 2 : 3 : 5 : 6-tetrachloronitrobenzene are labile. Products of amination isolated were 2 : 3 : 5 : 6-tetrachloroaniline and 3 : 5-*dichloro*-1-*nitro*-2 : 6-*diaminobenzene* (II); the presence of 3 : 5 : 6-trichloro-1-nitro-2-aminobenzene (I) was shown by reduction and conversion into 1 : 2 : 4-*trichloro*-5 : 6 : 9′ : 10′-*phenanthraphenazine*. Only the two chlorine atoms ortho to the nitro-group in 2 : 3 : 5 : 6-tetrachloro-4-nitroaniline (V) are labile; amination converted (V) into 3 : 5-*dichloro*-1-*nitro*-2 : 4 : 6-*triaminobenzene* (VI), and only a trace of 3 : 5 : 6-trichloro-1-nitro-2 : 4-diaminobenzene was detected by reduction and conversion into 1 : 2 : 4-*trichloro*-3-*amino*-5 : 6 : 9′ : 10′-*phenanthraphenazine*.

It was anticipated that the nitro-group in 2 : 3 : 5 : 6-tetrachloronitrobenzene would be more labile than the chlorine atoms in positions 2 and 6 and that the probable products of heating it with excess of alcoholic ammonia at 200° would be mainly 2 : 3 : 5 : 6-tetrachloroaniline, together with some 3 : 5 : 6-trichloro-1-nitro-2-aminobenzene (I) and 3 : 5-*dichloro*-1-*nitro*-2 : 6-*diaminobenzene* (II). When the product was distilled with steam, the non-volatile (II) was isolated in small amount, 2 : 3 : 5 : 6-tetrachloroaniline was recovered as the chief volatile constituent, but no (I) was isolated. The presence of (I) was demonstrated by first reducing a portion of the volatile product and then condensing it with 9 : 10-phenanthraquinone in acetic acid, 1 : 2 : 4-*trichloro*-5 : 6 : 9′ : 10′-*phenanthraphenazine* being formed.

In confirmation of its constitution, (II) did not condense with 9 : 10-phenanthraquinone, so it is not 5 : 6-dichloro-1-nitro-2 : 3-diaminobenzene. Reduction gave a triamine which condensed with 9 : 10-phenanthraquinone to give (III), so (II) is not 2 : 6-dichloro-1-nitro-3 : 5-diaminobenzene. Consequently, this triamine must be either 4 : 6-dichloro-1 : 2 : 3-triaminobenzene or 3 : 6-dichloro-1 : 2 : 5-triaminobenzene. Synthesis of the former *via* 3 : 5-dichloro-1 : 2 : 6-trinitrobenzene failed, because 3 : 5-dichloro-1 : 2-dinitrobenzene (Blanksma, *Rec. Trav. chim.*, 1908, **27**, 46) was recovered unaltered even after heating with potassium nitrate and 25% oleum at 130—160°. On the other hand, 2 : 5-dichloro-4 : 6-dinitroaniline was reduced by aqueous-alcoholic sodium hydrosulphite to 3 : 6-dichloro-1 : 2 : 5-triaminobenzene, which condensed with 9 : 10-phenanthraquinone to give 1 : 4-*dichloro*-2-*amino*-5 : 6 : 9′ : 10′-*phenanthraphenazine* (IV). The phenanthraphenazine (III) was isomeric and not identical with (IV). Compound (II), therefore, is 3 : 5-dichloro-1-nitro-2 : 6-diaminobenzene and (III) is 2 : 4-*dichloro*-1-*amino*-5 : 6 : 9′ : 10′-*phenanthraphenazine*.



(III.)

Amination of 2 : 3 : 5 : 6-tetrachloro-4-nitroaniline (V) furnished as main product the very stable 3 : 5-*dichloro*-1-*nitro*-2 : 4 : 6-*triaminobenzene* (VI) (the constitution of which is confirmed by the fact that it does not condense with 9 : 10-phenanthraquinone), only a trace of 3 : 5 : 6-trichloro-1-nitro-2 : 4-diaminobenzene being formed. Although the latter was not isolated, its presence was demonstrated, after separation of (VI), by reducing the residue, which consisted mainly of unaltered (V), and condensing the product with 9 : 10-phenanthraquinone, a little 1 : 2 : 4-*trichloro*-3-*amino*-5 : 6 : 9′ : 10′-*phenanthraphenazine* thus being obtained.

Experimental.

Microanalyses were carried out by Dr. G. Weiler and Dr. F. B. Strauss, of Oxford.

Amination of 2 : 3 : 5 : 6-*Tetrachloronitrobenzene: Formation of* 2 : 3 : 5 : 6-*Tetrachloroaniline*, 3 : 5 : 6-*Trichloro*-1-*nitro*-2-*aminobenzene* (I), *and* 3 : 5-*Dichloro*-1-*nitro*-2 : 6-*diaminobenzene* (II).—2 : 3 : 5 : 6-Tetrachloronitrobenzene (8·3 g.) and 2·94N-alcoholic ammonia (30 c.c.) were heated in a sealed tube at 200° for 10 hours, and the mixture distilled with steam. The reddish solid (6·4 g.) from the distillate was reduced with boiling aqueous-alcoholic sodium hydrosulphite; the mixture cooled and diluted, and the almost colourless precipitate collected, dissolved in acetic acid, and boiled with 9 : 10-phenanthraquinone in acetic acid for several minutes. The resulting precipitate (A) of 1 : 2 : 4-*trichloro*-5 : 6 : 9′ : 10′-*phenanthraphenazine* crystallised from amyl alcohol in pale yellow, fibrous needles, m. p. 262—263° [yield, 1·15 g., corresponding to a yield of 0·75 g. or 9·7% of (I)] (Found: N, 7·6; Cl, 26·8. $C_{20}H_9N_2Cl_3$ requires N, 7·3; Cl, 27·8%). The filtrate from (A) was diluted, and the precipitate collected; after removal of the phenanthraquinone with sodium bisulphite, 2 : 3 : 5 : 6-tetrachloroaniline crystallised from alcohol in colourless needles, m. p. and mixed m. p. 107—108° (yield, 4·5 g.; 61·2%). The non-volatile residue was crystallised from ligroin; 3 : 5-*dichloro*-1-*nitro*-2 : 6-*diaminobenzene* separated in fine, deep red needles, or scarlet leaflets, m. p. 172—173° (yield, 0·4 g.; 5·6%) (Found: C, 32·6; H, 2·2; N, 18·1; Cl, 31·5. $C_6H_5O_2N_3Cl_2$ requires C, 32·4; H, 2·25; N, 18·9; Cl, 31·9%). Its *diacetyl* derivative crystallised from acetic acid in colourless prisms, darkening at 295° and melting at 315° (decomp.) (Found: C, 39·4; H, 3·2; Cl, 23·2. $C_{10}H_9O_4N_3Cl_2$ requires C, 39·2; H, 2·9; Cl, 23·2%).

3 : 5-*Dichloro*-1 : 2 : 6-*triaminobenzene*.—3 : 5-Dichloro-1-nitro-2 : 6-diaminobenzene (0·35 g.) was boiled with alcohol (30 c.c.), and aqueous sodium hydrosulphite added until completely decolorised. The mixture was concentrated, cooled, and extracted with ether, and removal of ether gave a residue which crystallised from alcohol in clusters of colourless needles, m. p. 121—122° (decomp.) (yield, 0·17 g.; 56%). The triamine (0·09 g.) was boiled with 9 : 10-phenanthraquinone in acetic acid and gave 2 : 4-*dichloro*-1-*amino*-5 : 6 : 9′ : 10′-*phenanthraphenazine* (III), which crystallised from amyl alcohol in fine, orange needles, m. p. 265° (yield, 0·11 g.; 64·7%) (Found: C, 66·0; H, 3·1; N, 11·65; Cl, 19·2. $C_{20}H_{11}N_3Cl_2$ requires C, 65·9; H, 3·0; N, 11·55; Cl, 19·5%).

2 : 5-*Dichloro*-4 : 6-*dinitroaniline* (cf. Chem. Fabr. vorm. Sandoz; E.P. 457,518).—A mixture (6·3 g.) of equal parts of nitric acid (*d* 1·52) and 100% sulphuric acid was added to 2 : 5-dichloro-4-nitroaniline (10·4 g.) in 100% sulphuric acid (50 g.) at −5°, and stirred at 0° for 1 hour. After pouring on ice, the precipitate was collected, washed with cold dilute sodium hydroxide solution, and crystallised from alcohol, forming orange-yellow needles, m. p. 170—171° (yield, 6·7 g.; 53%).

3 : 6-*Dichloro*-1 : 2 : 5-*triaminobenzene*.—2 : 5-Dichloro-4 : 6-dinitroaniline (1·3 g.) in 50% aqueous alcohol (80 c.c.)

was reduced by adding sodium hydrosulphite until decolorised. The solution was cooled, diluted, and extracted with ether, ether removed, and the triamine crystallised from aqueous alcohol, forming fawn needles (yield, 0·15 g.; 16%), which were immediately condensed with 9 : 10-phenanthraquinone in acetic acid. 1 : 4-*Dichloro*-2-*amino*-5 : 6 : 9′ : 10′-*phenanthraphenazine* (IV) crystallised from amyl alcohol in small yellow needles, m. p. *ca.* 322° (yield, 0·25 g.; 83%) (Found : C, 66·2; H, 3·3; N, 11·5; Cl, 19·0. $C_{20}H_{11}N_3Cl_2$ requires C, 65·9; H, 3·0; N, 11·5; Cl, 19·5%).

Amination of 2 : 3 : 5 : 6-*Tetrachloro*-4-*nitroaniline* (V) : *Formation of* 3 : 5-*Dichloro*-2 : 4 : 6-*triaminobenzene* (VI) *and* 3 : 5 : 6-*Trichloro*-1-*nitro*-2 : 4-*diaminobenzene*.—2 : 3 : 5 : 6-Tetrachloro-4-nitroaniline (2·76 g.) and 2·94N-alcoholic ammonia (15 c.c.) were heated in a sealed tube at 200° for 22 hours. The contents of the tube were crystallised from alcohol; the solution deposited red needles (1·13 g.), m. p. 256—257° (decomp.). A further amount (0·2 g.) was obtained by diluting the alcoholic filtrate with water, collecting the precipitate, extracting it with hot concentrated hydrochloric acid, and diluting the acid extract with water. 3 : 5-*Dichloro*-1-*nitro*-2 : 4 : 6-*triaminobenzene* crystallised from alcohol in red needles, m. p. 256—257° (decomp.) (yield, 56%) (Found : C, 30·0; H, 2·9; N, 23·3; Cl, 30·5. $C_6H_6O_2N_4Cl_2$ requires C, 30·4; H, 2·5; N, 23·6; Cl, 29·9%). The yellow residue insoluble in hot concentrated hydrochloric acid consisted mainly of 2 : 3 : 5 : 6-tetrachloro-4-nitroaniline, but the presence of a trace of 3 : 5 : 6-trichloro-1-nitro-2 : 4-diaminobenzene was demonstrated by reduction with aqueous-alcoholic sodium hydrosulphite, dilution with water, and boiling of the resulting precipitate with 9 : 10-phenanthraquinone in acetic acid. 1 : 2 : 4-*Trichloro*-3-*amino*-5 : 6 : 9′ : 10′-*phenanthraphenazine* crystallised from acetic acid in clusters of light yellow needles, darkening at 280°, m. p. > 330° (yield, 1%) (Found : N, 10·9. $C_{20}H_{10}N_3Cl_3$ requires N, 10·55%).

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154. *Rare Earths in Scheelite.*

By JOSEPH K. MARSH.

Servigne's micro-method for the detection of rare earths by their luminescence in fused calcium tungstate gave high results for the more efficient luminophores when applied to natural scheelite. Only 5% of the reported abundance of europium in scheelite from Forbes Reef was found by chemical and spectroscopic analysis. Absorption bands of neodymium are also unusually intense in this mineral.

SERVIGNE (*Compt. rend.*, 1940, **210**, 440) reports 0·05—0·1% of europium in scheelite from Forbes Reef, Swaziland. As this would constitute an unsurpassed natural concentration of europium, together with a degree of segregation from other rare earths not before observed, and as the chemistry of its isolation would be easy, his findings have been tested by direct chemical means. He employed a micro-method, photographing the luminescence spectrum of a coating of scheelite on the interior of a discharge tube with argon and mercury filling and thus excited chiefly by Hg λ 2537 (*ibid.*, 1937, **204**, 863; 1938, **207**, 905; 1939, **209**, 210; *Bull. Soc. chim.*, 1940, **7**, 121). In the last paper he claimed that in calcium tungstate, by his technique and contrary to usual experience, each of several luminophores gives a reliable quantitative indication of its abundance over a wide range of low concentrations in presence of the others. This finding for artificial scheelite prepared at 1100° was applied to 15 samples of natural mineral of which the origin would be hydrothermal or pneumatolytic. The abundance of the earths found by him throws doubt on the validity of his assumption that natural scheelite behaves similarly as a base for luminescence to the artificial product. The fact that he found both to show identical *X*-ray patterns is not sufficient ground for this assumption. The luminescence depends upon the presence of 10^{-3}—10^{-5}% of rare earth and upon the situation of the earths at points of lattice defect. The necessary degree of defect is therefore below anything detectable by *X*-ray methods. He gives the effective decreasing order of luminophore strength in artificial scheelite as follows :

	Sm.	(Eu	Pr).	(Tb	Dy).	(Er	Tm).	Nd.	Gd.	
(*a*)	3(9)	2(6)	1(3)	(0)	(4)	(0)	(0)	(2)	(2)	
(*b*)	100	500	100	1	10	<1	—	—	—	$\times 10^{-4}$ %
(*c*)	25	25	10	10	80	15	—	50	65	$\times 10^{-4}$ %

In line (*a*) is given the number of times each rare earth was found by him to be the most abundant (or, in brackets, of unsurpassed abundance) in one or other of the 14 out of 15 natural scheelites which he found to contain rare earth. His estimate of the amount of each in Forbes Reef scheelite, in line (*b*), is compared with the author's, from chemical and spectroscopic analysis, in line (*c*). It is apparent from (*a*) that Servigne does in fact estimate those earths which he finds to be the best luminophores to be the most abundant in natural scheelites. His estimate for Forbes Reef earths differs very widely from the author's through an over-estimation of the strong luminophores. His estimates, moreover, show little of the coherence of the rare earths as a group which is always found in natural sources; *i.e.*, there is usually no great divergence from a certain proportionality between one earth and its neighbours in atomic number sequence, though the cerium or yttrium group, or even the middle members may predominate. Much the least coherent member of the group is, however, europium, which owing to its comparatively strong bivalence has become separated to the extent of about 80% in essentially rare-earth minerals, which are always of magmatic origin, and is found as a more widely distributed trace element in commoner minerals. The proportion to samarium found by the author in Forbes Reef scheelite is 80—100 times greater than in Travancore monazite and a few times greater than its probable lithospheric ratio (Goldschmidt, J., 1937, 655). Similar comparatively high europium proportions have been found in the rare earths from some pitchblendes (Marsh, *Phil. Mag.*, 1929, **7**, 1005).

Ordinarily the absorption coefficient of a rare earth is nearly constant in strength in presence of other rare earths, or in varying chemical combinations, but in Forbes Reef scheelite a much more intense absorption spectrum than usual is found. The orange neodymium bands 5850 and 5740 A. are, for the extraordinary ray, about 20 times more intense than is usual for solution bands in this region, *i.e.*, the augmentation is of a similar order to that of the luminescent power of europium in this mineral over the artificial product.

Experimental.

Isolation of the Rare Earth from Scheelite.—The ground mineral was freed from magnetic impurity, treated with dilute acid to remove a little calcite, and then added (45 g.) to fused sodium hydroxide (80 ml.). The cooled mass was lixiviated, and the solution filtered. The residue was dissolved in dilute nitric acid (400 ml.) in very slight excess, and the solution decanted or filtered from a small residue. Sodium hydroxide was then added dropwise till a precipitate formed. This was taken up in nitric acid, and a slight hydrogen sulphide precipitate removed. The solution was then reprecipitated with sodium hydroxide, and again taken up in nitric acid. After two oxalate precipitations a yield of 21 mg. of rare-earth oxides was obtained.

Another 50 g. of mineral were treated with successive quantities of hydrochloric acid till it was decomposed. The acid was evaporated, nitric acid added, and this evaporated. Water was added, the solution decanted from tungstic acid, and the rare earth recovered by hydroxide and oxalate precipitations as before. This was compared by arc spectroscopy with the previous yield. The rare-earth mixtures appeared identical. The former method of isolation is to be preferred. The two yields were united and again precipitated as oxalate. Yield, 45 mg. of oxides = 0·05% in the mineral.

Spectra of the Forbes Reef Scheelite Rare Earths.—(1) *Arc.* Lanthanum and lutecium were not found and there was only a trace of ytterbium. Yttrium, gadolinium, and dysprosium were found in considerable quantity. Europium appeared to exceed 3%. Cerium, praseodymium, neodymium, samarium, and terbium were identified. (2) *Absorption.* Neodymium gave the predominant spectrum: 20 mg. of oxide in 2 ml. of solution gave absorption bands equal to 1 g./l. of neodymia in solution. The neodymium content in the rare earth is therefore 10%. Erbium and holmium absorption bands were also identified on examining 20 mg. of oxides in 0·05 ml. of solution through 5 cm.

On the basis of the spectrum analysis and on general grounds of coherence of the group the estimate (*d*) was made. A mixed oxide was then prepared from pure materials to the composition of (*d*) and its arc spectrum compared with the scheelite extract. On the basis of this comparison a revised estimate (*e*) of the composition of the scheelite extract was made, the chief difference being a reduction in the estimate for cerium.

	Ce.	Pr.	Nd.	Sm.	Eu.	Gd.	Tb.	Dy.	Ho.	Y.	Er.
(*d*)	15	2	10	5	5	12	2	12	2	32	3 %
(*e*)	7	2	10	5	5	14	2	15	2	35	3 %

Luminescence of Scheelites.—A comparison of the cathodoluminescence of a number of scheelites was made with the aid of a Hilger constant-deviation spectroscope in order to determine if the Forbes Reef scheelite used by Servigne and by the author had comparable luminescent properties. The most striking feature found in the Forbes Reef luminescence was a pair of narrow bright red emission bands 6160 and 6120 A, identified as due to europium. They were less brilliant in a Rhodesian scheelite but were not seen in samples from Cumberland, Nevada, Bern, Bohemia, Piedmont, and Rhodesia (Mazoe Mine). They establish the similarity of the author's sample to Servigne's. The Forbes Reef scheelite gave the brightest luminescence of any sample examined. Observations on Bohemian and Piedmont specimens confirmed that the author's technique, although different from Servigne's, gave indications of similar relative abundances of the rare earths, *e.g.*, high samarium but little europium in the Piedmont specimen, and not much rare earth in the Bohemian specimen.

Absorption Bands of Scheelite.—The absorption bands 5850 and 5740 A. for the extraordinary ray found by Becquerel (*Ann. Chim. Phys.*, 1888, **14**, 170) were detected in 1·6 mm. of Forbes Reef scheelite. In solution the minimum concentration which the same spectroscope could detect was 1 g./l. of neodymia in 1 cm. thickness. The neodymium content of the scheelite has been shown to be 5×10^{-3} %, or 3×10^{-1} g./l., and the bands were detected in 1·6 mm., equivalent to 1 cm. of $0{\cdot}5 \times 10^{-1}$ g./l., or 20 times less than the minimum required for detection in solution.

Mr. C. T. Pott, of The Union Corporation Ltd., is thanked for obtaining the sample of Forbes Reef scheelite.

The Inorganic Chemistry Laboratories, University Museums, Oxford. [*Received, September 14th*, 1943.]

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155. *The Solid Product of Carbonisation.*

By G. Milner, E. Spivey, and John W. Cobb.

Properties capable of numerical evaluation of the solid product of carbonisation (coke) from a variety of materials have been studied. True specific gravity reached approximately 1·4 at 500° and 1·8 at 800°, with very slight further change to 1200°. The absence of progress to 2·25, the specific gravity of graphite, is attributed to gas (which escapes very slowly) between the layers of graphitic crystallites. The identity of substance indicated by that of specific gravity (1·85) is obscured by the varying formation of superficial graphitic films. Oxygen remaining in the substance carbonised is held responsible for the subsequent gasification from 500° upwards of nuclear carbon (see J., 1942, 252), and for the formation of an intimately pervasive micro-capillary system indicated by absorption of carbon dioxide. The terminations of these capillaries at a surface increase its rate of gasification and the reactivity of the coke. Hence, there is a causal connection between oxygen content of the material carbonised, micro-porosity or adsorption of carbon dioxide by a coke and its reactivity, and these often lie in the same order, but not necessarily so, as explained. Increasing the surface of a coke by carbonising it with admixed inert material increased reactivity but not adsorption. The micro-capillarity developed in carbonisation reached a maximum at 800—1000° and then diminished. The influence of soda and equimolecular quantities of other inorganic materials in increasing reactivity was compared and discussed.

In a typical example of that gradual progress of a carbon compound towards carbon under the influence of rising temperature known as carbonisation, there is at each temperature stage a loss of volatile matter (gaseous

or liquid), and an adjustment of internal molecular structure, leaving a solid product. The liquid products are of great variety according to the material carbonised, and their expulsion is complete at about 600°. The primary gaseous products have already been examined (*loc. cit.*) and the study of the solid product is now reported.

Specific Gravity.—One change in the solid product, or coke, as the temperature rises, is in specific gravity, and Table I displays results obtained for some substances differing in constitution and behaviour on carbonisation. The method of determination was the same in each case (Greenwood and Cobb, *J. Soc. Chem. Ind.*, 1922, **41**, 181), materials low in ash being chosen to minimise its effects on specific gravity. The description of coals is that of Seyler's classification. [In a rapid laboratory carbonisation to 800° of filter-paper and

TABLE I.

Changes in specific gravity.

A. Cellulose (filter-paper), infusible (ash, <0·01%); prolonged fractional carbonisation in a vacuum: 24 hrs. at specified temperature.
B. Welsh ortho-anthracite, Stanllyd, infusible (ash, 0·92%)
C. Welsh meta-bituminous coal, Black Vein, fusible (ash, 1·84%)
D. Notts. para-bituminous coal, New Hucknall, less fusible (ash, 3·77%)

} carbonised by raising temperature at 5°/min., and 3 hrs. at specified temperature.

Specific gravity of cokes prepared at various temperatures.

	15°.	200°.	300°.	400°.	500°.	600°.	700°.	800°.	850°.	900°.	1000°.	1100°.	1200°.
A	1·60	1·61	1·41	1·38	1·42	1·59	1·70	1·82	—	1·82	1·86	1·86	1·85
B	1·44	—	—	1·45	1·45	1·49	1·63	1·76	1·80	1·83	1·71	1·70	—
C	1·29	1·29	1·30	1·34	1·40	1·50	1·64	1·77	1·80	1·85	1·86	1·87	—
D	1·27	—	—	—	1·59 *	—	—	—	1·87	—	—	—	1·88

* At 550°.

cotton-wool (both infusible) and cane-sugar (easily fusible), the specific gravities of the residues were rather lower than were obtained in the much slower carbonisations reported above, but were practically identical (*viz.*, 1·61, 1·62, 1·65 respectively).]

Anderson (*ibid.*, 1896, **15**, 20) found for various by-product cokes *d* 1·83, 1·85, and 1·88. Drakeley and Wilkins (*ibid.*, 1931, **50**, 333), after stamping a finely powdered typical Durham gas-coal at 10 tons/sq. in. and carbonising it at various temperatures until gas evolution had ceased, obtained cokes of *d* 1·49, 1·91, 1·94, 1·92, and 1·94 at 450°, 800°, 960°, 1000°, and 1100°, respectively, but, the ash content of the cokes being approximately 12%, the specific gravity of the ashless coke would be rather lower; *e.g.*, if a coke of *d* 1·91 contained 10% of ash of *d* 2·5 (which may well be exceeded by a ferruginous ash), the ashless coke would have the same specific gravity (1·85) as the mean of the values reported for cellulose and other cokes from 800° upwards in Table I. Smith and Howard (*Ind. Eng. Chem.*, 1942, **34**, 438) found an average value for American commercial high-temperature cokes as determined in water to be 1·9, while 525° coke gave 1·47, 700° coke 1·85, and 1000° coke 1·92. Here again necessary allowance for ash would lower the figures.

In examining the course followed by the specific gravity of the carbonised materials, as determined in our laboratory (Table I) (and consistent with results quoted from other sources), three stages are noticeable which are connected with the changes discussed by Bolton, Cullingworth, Ghosh, and Cobb (J., 1942, 252): (1) Up to 500° the alterations in specific gravity varied with the material carbonised, as did also the gaseous and liquid products, until a common *d* value of approx. 1·4 was attained at 500°. (2) From 500° up to 800°, the specific gravity rose steadily for each material to a common value near 1·8. The primary gaseous products in this stage were first methane, then hydrogen and (from oxygenated substances) carbon monoxide, and the chemical mechanism suggested was for each gas one of condensation of the type $R_1H + CH_3R_2 \longrightarrow R_1R_2 + CH_4$, where R_1 and R_2 were the newly formed, or in some cases pre-existent, benzenoid groups. (3) From 800° up to 1200°, the limit of our work (and approximately of industrial carbonisation), no further increase in specific gravity beyond 1·85 was established. Occasionally, there was a slight diminution, as found for anthracite, presumably due to the formation of closed micro-pores or fine micro-capillaries not penetrated by water in the specific-gravity determination. There was no appreciable progress towards 2·25, the density of crystalline macro-graphite. This stage of a practically constant specific gravity of 1·85 was marked by continuing emission of hydrogen and carbon monoxide.

Dr. W. T. Astbury's *X*-ray examination had shown that in the carbonised cellulose residues the two most characteristic rings as given by graphite, denoting the formation of hexagonal networks of carbon atoms in the parallel sheets of graphitic crystallites, appeared at 500°. This followed on an earlier general diffuseness which indicated a breakdown of the original structure, and some diffuseness in the rings themselves, arising from small or imperfect crystals, persisted even at 1200°.

The rapid molecular condensation in the solid, with its accompanying free escape of gas, from 500° up to 800° had been marked by pronounced increase in specific gravity. The distinguishing feature of gas emission in the stage from 800° to 1200° was its long, slow continuation over many days even under vacuum. Completion of emission at these temperatures was indeed not secured, as noted when dealing specially with the primary gaseous products. This gas, so difficult to expel, was presumably held between the sheets of the crystallites, and would prohibit that approach of the sheets to one another necessary for increase of specific gravity. The fixation of interplanar hydrogen and its effects have been investigated by H. L. Riley. It is

significant that only after this 800—1200° stage does the growth of crystallites in the direction at right angles to the hexagonal-patterned planes, commence (Blayden, Riley, and Taylor, *J. Amer. Chem. Soc.*, 1940, **62**, 180). The important point for our immediate purpose is the failure of the specific gravity to exceed 1·85 even at 1200°: a much higher temperature seems to be necessary for complete graphitisation, and the corresponding specific gravity of 2·25.

Surface Film.—Account must, however, be taken of the condition of the surface film as distinct from the whole carbonised substance, and in order to do this we must consider the equilibrium $CO_2 + C \rightleftarrows 2CO$ when carbon dioxide is circulated over the surface. It has been shown (Dent and Cobb, J., 1929, 1903) that at 800° this equilibrium is conditioned by the nature and heat treatment of the "carbon" surface. The following results are relevant: (i) With coco-nut charcoal, formed without fusion, the equilibrium mixture obtained after prolonged circulation of carbon dioxide at 800° contained 9·15% of this gas when the charcoal had been previously heated for 22 hours at 900° in a vacuum, 10·7% when heated for 50 hours at 900°, and 12·10% after 48 hours' heating at 1010°. (ii) With coke from Sharlston Wallsend (Haigh Moor) coal formed with fusion (which would facilitate molecular rearrangement in a more stable form at an early stage, lending itself to graphitisation on the surface where interplanar hydrogen cannot be effective at a higher temperature), the equilibrium at 800° after 50 hours' previous heating at 900° was at 13·8% of carbon dioxide, and the same value was given by Ceylon graphite. (iii) When the graphitised surface film had been removed by slight gasification, the interior mass gave a lower equilibrium content of carbon dioxide and a higher velocity of gasification in a stream of the gas, corresponding with its structure.

The essential identity of the molecular structure formed from different substances throughout the range 800—1200° may therefore be obscured by differences in the surface films (although these are too thin appreciably to affect the specific gravity), and all the more so because the surface film usually displays its properties from the first in any reaction studied. As soon, however, as we leave the fundamental property of specific gravity, the various carbonised products display their differences in such measurable properties as porosity, powder density, surface, adsorptive power, and reactivity. These properties, *e.g.*, in the region 800—1200°, where specific gravity shows so little change, vary widely.

Percentage Porosity.—This property gives some indication of surface, although indirectly and imperfectly, since the numerical value obtained is different according to the method of determination. A porosity due to micro-capillaries can be calculated from the results of two specific-gravity determinations—one made by using water (or helium), and the other mercury, a liquid which does not penetrate micro-capillaries below some 6 μ in diameter at N.T.P. (Smith and Howard, *loc. cit.*). The results obtained by this method (Table II) show the comparative behaviour of the anthracite and meta-bituminous coals (B and C) of Table I in the same carbonisation as provided samples for the determinations there reported (Lane, Thesis, Leeds, 1934).

TABLE II.

Micro-porosity after carbonisation at various temperatures, %.*

Coal (see Table I).	15°.	400°.	500°.	600°.	700°.	800°.	850°.	900°.	1000°.	1100°.
B	3·03	4·8	4·7	5·1	7·4	9·8	11·9	9·9	3·1	1·0
C	1·00	5·8	14·7	17·9	18·8	20·8	20·6	18·6	17·3	14·9

* Porosity % $= 100(d_{H_2O} - d_{Hg})/d_{H_2O}$.

It will be noted that the fusible coal increased greatly in micro-porosity between 400° and 500°, and that both coals reached a maximum porosity at 800—850°, and then showed a decline.

A method of dealing with a grosser pore system consists in dipping a lump of coke in molten paraffin-wax, allowing it to drain, and then weighing it in air and in water. By this method applied to three coals, each carbonised at a series of temperatures ranging from 500° to 800°, substantially the same result was obtained throughout, *viz.*, a porosity of about 55% ("The Solid Products of Carbonisation of Coal," South Met. Gas Co., 1934, p. 36).

Powder Density.—This property is useful in marking, *e.g.*, the much greater bulkiness and surface area of paper coke than of sugar coke, although these have the same specific gravity. The adsorption of a unimolecular layer of methylene-blue from solution is sometimes used as a measure of surface, it being assumed that 1 mg. of the dye corresponds to 1 sq. m. of surface (see Table III and cf. Paneth and Radu, *Ber.*, 1924, **57**, 1221).

Adsorptive Power for Carbon Dioxide.—This is one of the properties capable of numerical expression which has best repaid study: in Table IV is arranged a series of substances in order of descending oxygen content, and in other columns the adsorption values for carbon dioxide at 20° and reactivities to this gas of their cokes at 900°. A wide range of materials was examined including cokes prepared from pure substances of known constitution rich in oxygen and of very low ash content, as well as from coals of the principal types, petroleum coke, retort carbon, graphite, etc. The adsorption as estimated was a reversible secondary adsorption at 20° in c.c. of the gas (calculated to 20° and 760 mm.) per g. of powdered carbonised residue. Its magnitude will be determined by the extent of the micro-capillary system existing in the residue tested, and also by the nature of the surface. In making the estimation, not only is the total adsorption, V, determined, but also that during the first ½ hour; the latter, being expressed as a percentage, R, of the total adsorption, gives some measure of the rate of adsorption: R may diminish without appreciable alteration in V if surface graphitisation lessens ease of access of the gas to the interior of particles otherwise unchanged. This type of adsorption in micro-

capillaries is confined to pores of diameter less than 12 μ (Harkins and Ewing, *J. Amer. Chem. Soc.*, 1921, **43**, 1787).

Oxygen Content and Adsorption.—Attention may be directed first to the highly contrasted adsorption (in c.c./g.) and rate of adsorption in various gases of some cokes from materials, four of very high, and two of low,

TABLE III.

Oxygen content and adsorption of gases.

Material.	O_2, %, in material.	Material.	O_2, %, in material.
A. Cellulose (filter-paper)	49·4	D. Starch	—
B. Cellulose (cotton-wool)	49·4	E. Black Vein coal	3·7
C. Sugar	51·5	F. Petroleum coke	<1·0

	Adsorption by cokes, c.c./g.								Surface, $m.^2/g.$, by M-B.	Powder density of cokes, g./c.c.	Sp. gr. of cokes.
	CO_2.		SO_2.		H_2.		O_2.				
	V.	*R.*	*V.*	*R.*	*V.*	*R.*	*V.*	*R.*			
A	45·5	100	89·0	94	1·5	75	8·3	100	6·0	0·15	1·61
B	45·0	100	85·0	98	6·9	trace	8·5	100	14·0	0·07	1·62
C	47·0	100	86·6	96	4·0	17	7·4	100	0·7	0·40	1·65
D	46·5	97	—	—	—	—	—	—	0·6	—	—
E	5·2	22	—	—	—	—	—	—	—	—	—
F	8·7	31	—	—	—	—	—	—	—	—	—

oxygen content. The high values with carbon dioxide, as compared with hydrogen and oxygen, are presumably obtained because the determinations are made below the critical temperature of the dioxide (31°). This is emphasised by the still higher results with sulphur dioxide, which has an even higher critical temperature (157°). Carbon dioxide was used throughout in our survey.

Most significant is the practical identity of adsorption given by the cokes from paper, cotton-wool, sugar, and starch, although the last two substances fused early in carbonisation, whereas the first two gave no sign of fusion at any stage and displayed the greater bulkiness and surface indicated by low powder density and high adsorption of methylene-blue. This high and identical adsorption seems to mark the formation of remarkably similar micro-capillary systems from these substances rich in oxygen. The contrasted low adsorption of Black Vein and petroleum cokes suggests that oxygen is a necessary agent in the formation of any developed micro-capillary system. The practical identity of adsorption of the cokes from paper (45·5), cotton-wool (45·0), sugar (47·0), and starch (46·5), prepared by very rapid (20 mins.) carbonisation at 800°, was confirmed by the values obtained on much slower carbonisation (3½ hours), *viz.*, 56·0, 57·0, and 58·0 for the first three respectively (see Table IV).

The formation of so similar a micro-capillary system from these fusible and infusible substances rich in oxygen would suggest that it was brought into being after a point in carbonisation had been reached at which the state of the relevant units of each substance was so far the same that subsequent treatment had the same effect. This implies that in the fusible substances the micro-capillary structure came into being after the stage of fusion had been completed with the formation of such a solid residue as was also forthcoming from the infusible substances. It is plain that, although in some other respects the solid residues from the fusible and the infusible substances might then be quite different, yet they were the same for the development of micro-capillarity. As to how this marked development was effected, a clue is provided by the fact that it occurred only in substances rich in oxygen, being present to the same extent in the cokes from paper, cotton-wool, and sugar, to nearly the same extent in cokes from oxygen-rich coals (see Table IV), but to a diminishing degree in those from materials poorer in oxygen, such as anthracite, and hardly at all in such hydrocarbon residues as petroleum coke, pitch, and retort carbon. The mode of action of the oxygen, if it is responsible for the micro-capillary structure, needs explanation. Some of the original oxygen is not effective, but is expelled in various combinations quite early. There is, however, as already indicated (J., 1942, 252), a second stage in carbonisation, from 500° upwards, marked by the evolution of oxygen in combination with carbon (mainly as the monoxide). This removal of carbon may well be responsible for the micro-porosity. The mechanism there suggested was a condensation such as $R_1{\cdot}OH + R_2H \longrightarrow R_1R_2 + H_2O$, followed by the attack of the steam so generated on carbon. It was also suggested that the carbon surviving to this stage of carbonisation was mainly nuclear aromatic carbon, so that the action of oxygen by such a mechanism would be of an intimately pervasive character affecting atomic configurations. If this view is correct, the micro-capillary structure is developed by the action of that part of the oxygen in the substance carbonised which remains in the solid carbonised residue when the first stage of carbonisation is complete, and it acts by the removal of nuclear carbon, mainly as monoxide. [Work carried out at Leeds by F. J. Dent and others for the Joint Research Committee (43rd Report, *Trans. Inst. Gas Eng.*, 1938—9) has shown that, in hydrogenation under 50 atm., nuclear carbon may be gasified readily as methane by hydrogen, in which special case a micro-capillary system could be formed without the intervention of oxygen. Under normal carbonisation conditions, however, this only occurs to a slight extent, so oxygen remains as determining in effect the gasification of nuclear carbon.]

As an illustration, attention was directed (J., 1942, 252) to a difference in behaviour between two coals,

New Hucknall and Sharlston Wallsend, subjected to fractional carbonisation. They differed somewhat in oxygen content but quite disproportionately so in the emission of oxides of carbon, the latter coal giving only about a fifth as much as the former, the low-temperature emission being small from both. " A difference in antecedent molecular condensation during formation " of the coals was then held responsible, " leading to a greater survival of firmly attached ·OH groups " in the New Hucknall coal during carbonisation. The Sharlston Wallsend coke as now tested for adsorption of carbon dioxide (Table IV) gave a much lower value (7) than the New Hucknall coke (27).

Reactivity.—Probably the most important influence of adsorptive power for carbon dioxide is on the reactivity or comparative rates of gasification in a current of gas, such as carbon dioxide, steam, or oxygen which goes so far to determine the behaviour of a carbonised residue when used as fuel. Various methods of defining and determining reactivity for this purpose have been adopted. The one we have used was first described by Branson and Cobb (*Trans. Inst. Gas Eng.*, 1927, 357) and discussed in detail by Key and Cobb (*J. Soc. Chem. Ind.*, 1930, **49**, 439T). Unit reactivity is represented by a decomposition of 20% of carbon dioxide passed at the rate of 5 l./hr. over 10 g. of the material. The specific reactivity as determined at 900° in terms of this unit is the most generally useful value, the material being sized to pass a $\frac{1}{8}$" but not a $\frac{1}{10}$" sieve and being contained in a tube of $\frac{7}{8}$" diameter. If the percentage of gas decomposed by weights 1 and n of a coke A are X and X_n, then X_n represents a reactivity n times that of X; therefore, by finding X_n experimentally for different values of n, a curve can be constructed connecting reactivity with percentage decomposed, from which the reactivity of any coke can be found when the percentage decomposition has been determined. This having been done by trial, the experimental curve so determined was found to coincide with one constructed on the supposition that the reaction was of the first order, and the following formula is applicable:

$$R = 7{\cdot}35(V/w)[-\ 9{\cdot}2\log_{10}(1-x) - \tfrac{1}{2}x^2 - 3x]$$

in which R = specific reactivity, w = weight (in g.) of coke, V = the velocity of the carbon dioxide in l./hr., (N.T.P.), and $100x$ = percentage of carbon dioxide decomposed. The extent of decomposition of the gas effected in such a determination at, say, 900° will depend at any time on the nature of the surface exposed (as would be indicated, *e.g.*, by the equilibrium value in the reaction $C + CO_2 \longrightarrow 2CO$), on the extent of the surface over which the gas flows, and on the action of a catalyst if one is present.

When gauging reactivity in this manner, it might appear that even slight variation in sizing would affect the result, but this obvious source of error proved on examination to offer much less difficulty than had been anticipated. Consistent results could be obtained with material sized as described above ($\frac{1}{8}$"—$\frac{11}{10}$"), and Jones, King, and Sinnatt (Dept. Sci. and Ind. Res., Tech. Paper No. 18) showed that the reactivity value they determined by a similar method did not increase to any extent with decreased size. In tests made later in our laboratory (H. Taylor, Thesis, Leeds, 1938) to ascertain the influence of particle size on reactivity to carbon dioxide, cokes made at 1000° from Haigh Moor fusible coal and from infusible anthracite were prepared in widely different sizes—from $\frac{1}{4}$—$\frac{1}{8}$" down to $\frac{1}{60}$—$\frac{1}{100}$". The value for specific reactivity at 900° of the Haigh Moor coke rose steadily from 0·39 for the former size to 0·53 for the latter, and that of the anthracite coke from 0·14 to 0·18. Such results for these extreme conditions confirmed previous experience, *viz.*, that the test as carried out with the standard sizing ($\frac{1}{8}$—$\frac{1}{10}$") or even with some variation from that standard would yield reliable results. The above reactivity test was usually continued for 2 hours, during which the weight of material steadily decreased by an amount (such as 10%) increasing with reactivity. If the specific reactivity remained constant during the gasification, the proportion of carbon dioxide decomposed in successive samples taken during the test would diminish in degree corresponding with the loss of weight, but actually the effective surface, on which the rate of gasification depends (and therefore the % of monoxide), usually remained substantially constant. This automatic adjustment often applies up to 50% gasification, but not always, and discretion must be used in deducing specific reactivity from the results.

In a normal test of reactivity, the gasification is limited to 120 mins. in carbon dioxide at (say) 900°, after 15 mins. in nitrogen, and gas samples taken after 5, 20, 40, 60, 90, and 120 mins. in carbon dioxide indicate period reactivities from which a mean decomposition or reactivity is deduced.

Oxygen and Reactivity.—If we assume that oxygen is responsible for the micro-capillarity indicated by high adsorption of carbon dioxide, does it thereby affect reactivity? The question arises because, of the gas flowing through the column of material under test for reactivity, only a small proportion can possibly follow the high-resistance paths offered by the micro-capillaries. Drakeley estimated it at some 2% after trials with cold air (*J. Soc. Chem. Ind.*, 1931, **50**, 321T). On the other hand, the hot gas impinging on any surface which is not continuous but the termination of multitudinous micro-capillaries, with their thin accessible containing walls, has its extent of attack enormously increased thereby. The mode of attack is not always the same. With some substances, with a uniformly fine capillary structure, the tendency is for the particles to diminish in size as removal of material is affected layer by layer. With other substances, coarser or less homogeneous in capillary structure, with macro- as well as micro-pores, the whole particle becomes honeycombed, with no obvious diminution in size until gasification is far advanced. Cokes prepared from coal often behave in this manner. It is then quite comprehensible how a well-developed micro-capillary system, itself due to oxygen as explained, lays the foundation as it were, for high reactivity, and why a substance of very low oxygen content gives normally an unreactive coke. Thus (see J., 1942, 252), a low-temperature petroleum coke (450°), with negligible oxygen content, gave only 5·8 c.c. of oxides of carbon during further carbonisation to 1000°,

whereas bakelite, containing 16% of oxygen, gave 154·3 c.c. (147·2 c.c. of which were monoxide) in the same temperature range (with a negligible volume below it); consequently, the reactivity to carbon dioxide at 900° of the carbonised product was low (0·14) for petroleum coke and high (3·0) for bakelite.

Total Surface.—Although oxygen, through the capillary system it induces, becomes the basis of reactivity, it is nevertheless the whole surface over which the gas flows which is directly and immediately responsible, and whatever increases this effective surface per g. of material under test increases reactivity. For instance, paper coke and sugar coke have the same high absorption for carbon dioxide, but although the latter, fused in formation, has a high reactivity (0·6) compared with anthracite coke (0·25) formed from material of low oxygen content, yet its reactivity compared with that of paper coke (2·7), formed without fusion, is low, presumably on account of the much smaller surface bounding its micro-capillary system. If, by any means, this surface were increased, a corresponding increase in reactivity would be expected. Experiments were, therefore, made in which a series of cokes was prepared from sugar alone and from sugar mixed with purified alundum to give a gradually increasing surface of deposition for the sugar-carbon produced on carbonisation; 30 g. of each blend were used for a test of reactivity, the exact amount of the carbon present being determined by ignition. As the ratio of alundum to sugar rose from 1 : 2 to 10 : 1, the corresponding specific reactivity of the contained carbon rose steadily from 0·92 to 2·02 (that of the sugar carbon alone being 0·64) and the surface (by methylene-blue) from 3 to 20 sq. m. per g. of carbon.

Similar increases in specific reactivity were obtained when glycine coke was increased in surface by blending with alundum or kaolin before coking. The carbon dioxide adsorption of the blended cokes made from sugar and diluent alundum (or silica, kaolin, or diatomaceous earth) was also determined. Here, no increase was noted, the carbon dioxide adsorption per g. of sugar coke in the mixture being always substantially the same as that of sugar coke itself. It was plain that the carbon micro-capillary system adsorbed the gas to the same extent, whether massed in sugar coke or dispersed on extended surface in a blend, but the micro-capillaries in the blend terminated on a much wider expanse of surface, leading to increased gasification and reactivity. On this view, a surface will always have some effect, but this is greatly increased when the surface is formed by terminating capillaries. (The inorganic diluents tested separately gave no adsorption.)

Survey of Materials.—It is now possible to compare (Table IV) the results of a wider survey of cokes, prepared from typical materials placed in descending order of oxygen content, with regard to adsorption and reactivity values. A series of coals is included covering Seyler's classification, and these were treated by flotation when necessary so as to bring the ash content to about 1% and minimise its possible disturbing influence. Cokes were also tested from coals which had been allowed (see below) to take up oxygen by exposure in the air-oven at 200° for 4 weeks. Reactivity was determined in carbon dioxide at 900° on materials carbonised in 3½ hours to 800°; *V* and *R* show total adsorption and rate as on p. 580 and in Table III.

TABLE IV.

Adsorptions and reactivities of cokes from different materials.

Material and resulting coke.	O_2, %,* before carbonisation.	Adsorption of CO_2, c.c./g. by sized cokes. 1/5—1/12". *V.*	*R.*	1/20—1/40". *V.*	*R.*	<1/60". *V.*	*R.*	Reactivity at 900°.†	Adsorption preoxidised. 1/5—1/12". *V.*	*R.*	1/20—1/40". *V.*	*R.*	Reactivity, preoxidised.	Ash, %, in material.
Cellulose (ashless filter-paper), not fused	49·4	—	—	56	100	57	100	2·67	—	—	—	—	—	<0·01
Sugar-coke, fused	51·5	—	—	58	100	57	100	0·60	—	—	—	—	—	<0·001
Cellulose (cotton-wool), not fused	49·4	—	—	57	100	57	100	6·7 (rapid c.)	—	—	—	—	—	0·10
Coco-nut shell (carbonised at 920°)	—	70	100	71	95	—	—	8·0 (10·5)	—	—	—	—	—	0·5
Lignite (Bovy Tracy), not fused, brown	27·6	51	93	49	100	—	—	6·29	—	—	47	100	6·7	1·1
Bakelite (formaldehyde resin)	16·2	—	—	—	—	—	—	3·04	—	—	—	—	—	0·2
New Lount, meta-lignitious, not fused, black	12·1	38	54	37	84	—	—	1·28	46	98	46	100	1·7	1·25
Warrenhouse, meta-lignitious, not fused, grey	9·6	33	66	32	87	—	—	1·72	—	—	44	100	2·0	1·25
New Hucknall para-bituminous, semi-fused, dull grey	9·0	—	—	27	49	—	—	1·32	—	—	44	93	1·6	1·0
Beamshaw, para-bituminous, fused, lustrous grey	8·4	27	24	24	49	—	—	0·45	—	—	44	77	0·73	0·6
Altofts	—	4·3	15	12	15	—	—	0·39	—	—	42	93	—	—
Black Bed, ortho-bituminous, silvery	6·3	3·2	18	7·7	4·5	—	—	0·31	—	—	40	66	1·3	1·9
Haigh Moor, ortho-bituminous (Sharlston Wallsend), fused, silvery	5·9	—	—	7·0	7·5	—	—	0·20	—	—	39	89	1·1	0·6
Lupset, meta-bituminous, fused, silvery	4·4	2·6	17	5·7	9·0	—	—	0·17	37	68	38	78	0·64	1·2
Black Vein, meta-bituminous, fused, silvery	3·7	—	—	5·2	22	16	43	0·04	—	—	30	83	0·39	1·1
Two Foot Nine, semi-bituminous, dull grey	2·5	14	51	18	43	—	—	0·20	—	—	31	79	0·34	0·6
Lower New, carbonaceous, not fused, black	1·7	10	25	12	61	—	—	0·12	30	68	28	75	0·22	1·9
Stanllyd anthracite, not fused, unaltered	1·6	15	17	21	56	30	85	0·20	—	—	—	—	—	3·5
Petroleum coke	<1·0	—	—	8·7	31	—	—	0·14	—	—	—	—	—	—
Gas-retort carbon (deposited from hot gas)	<1·0	—	—	0·5	0	—	—	lowest <0·02	—	—	—	—	—	1·0
Graphite	<1·0	—	—	0·2	0	—	—	0·02	—	—	—	—	—	1·0

* The oxygen before carbonisation is calculated in the materials free from moisture, sulphur, and ash.
† Cokes of reactivity below 0·2 at 900° may with advantage be compared at a higher temperature (cf. Table VI).

Discussion of Results from Table IV.—Oxygen in the materials before carbonisation, carbon dioxide adsorption of the cokes, rates of this adsorption, and reactivities have all at various times been suggested empirically

as lying in the same order. For reasons discussed above, such supposed parallelism would sometimes be quite misleading, but there is a causal connection and it is not surprising to find these properties with such a series of coals as that in Table IV (carbonised and tested under the conditions described) lying in nearly the same order. As judged by the values for V and R, it would appear that, with all the substances of high oxygen content, a micro-capillary system has been established by carbonisation which gives a rapid access and high adsorption of carbon dioxide; this effect is very much lessened in the fusible coals of low oxygen content from Black Bed (6·3%) downwards, increased again somewhat in the infusible carbonaceous coals, and finally almost obliterated in the substances with less than 1% of oxygen and very low reactivity. The lowest reactivity (with very low adsorption) was shown by gas-retort carbon. This is presumably due, not only to the negligible oxygen content of the gas from which it is formed, but also to its mode of formation—slow deposition by the decomposition of hot gas—which would facilitate the building up of a closely-knit, impervious carbon structure.

The comparative freedom of access of carbon dioxide was also brought out in the adsorption shown by materials of different sizing. It made no difference until the lower adsorptions (again from Black Bed downwards) were reached, but from that point onwards was noticeable. (It was suggested above that the cause of the fall in the true specific gravity of anthracite from 900° upwards, as determined in water, was the minute capillaries not penetrated by the water.)

Addition of Oxygen.—The foregoing study of the influence of oxygen contained in materials undergoing carbonisation was supplemented by experiments in which oxygen was added to coals directly, and the influence on the reactivity and adsorption of the cokes determined. For all the coals in Table IV, the results are given of passing air slowly over them for 4 weeks while they were heated in an air-oven at 200°, before carbonisation. In nearly every case marked increase in adsorption and reactivity of the coke resulted; the proportional increase was most pronounced with the coals of lowest oxygen content, but one striking result was the high and similar adsorption of carbon dioxide (40—47 c.c./g.) given by most of the cokes from the oxidised coals. The only exceptions showing little or no increase were lignite and anthracite, at the two ends of the series. Lignite may be presumed to be already so far provided with oxygen that the very little it fixed had no further effect. With anthracite, preliminary experiments showed that at 200° its oxygen fixation was practically nil, and this inertia may be explained by the extensive aromatic condensation which it had already undergone during formation, with development of graphitic crystallite structure (Blayden, Riley, and Taylor, *loc. cit.*). When heated at 325°, however, anthracite fixed 7·9% of oxygen in 27 hours and the cokes showed an increase in reactivity from 0·35 to 0·93 (at 950°). Heating in nitrogen caused no such increase. In another series of tube experiments, Haigh Moor bituminous coal was heated at 150° in air, with collection of the gases evolved, during periods increasing up to 12 hours, and the reactivities of the corresponding solid products after carbonisation determined. Parallel blank experiments were made using nitrogen instead of air, and the determinations corrected accordingly. The corrected results from oxidation of 100 g. of coal in these experiments after 12 hours were: total oxygen consumed, 4·07 g.; oxygen in water, 1·48 g.; in carbon dioxide, 0·39 g.; in carbon monoxide, 0·23 g.; fixed (by diff.), 1·97 g. The reactivities of the coked residues rose steadily from 0·5 to 0·9, but all those from the nitrogen "blanks" had the same reactivity as that from the untreated coal, *viz.*, 0·5, a result uniformly forthcoming in other similar tests.

It was noticeable that the loss of oxygen as carbon dioxide and water (3·3 g. in 12 hours) in treatment of the coal in nitrogen at this low temperature had no effect on the reactivity of the coke, but that oxygen taken up during the heating in air was more firmly fixed and had a marked effect in raising the reactivity of the coke, presumably by its expulsion of carbon as monoxide at a higher temperature, where it would influence the structure as suggested above. The maximum oxygen fixed (in 28 hours at 150°) was 3·89%, and the corresponding increase in reactivity of the coke was to 1·87. The coking property was practically destroyed at an early stage in the oxidation with only a slight increase (0·1) in reactivity, but both oxidation and reactivity continued to increase steadily. The same was noted with the other fusible coal (New Hucknall) similarly tested. [In view of the marked increase in reactivity brought about by oxygen, it was not surprising that 7 and 24 months' storage of a newly mined and powdered coal ($\frac{1}{6}$—$\frac{1}{10}$") raised the reactivity of the coke from 0·2 to 0·4 and 0·5 respectively.]

These results, obtained by the direct action of oxygen on bituminous coals, lignite, and anthracite (for further details, see G. Milner, Ph.D. Thesis, Leeds, 1933), are in full accord with the view expressed above from quite other considerations. The causal connections between oxygen content, adsorption, and reactivity so far indicated may be expressed as follows: oxygen remaining in the solid product after the first stage of carbonisation (sometimes including fusion) becomes responsible from 500° upward for the subsequent gasification of carbon, mainly as monoxide, and the consequent formation of an intimate micro-capillary system, which in such a process as gasification of the solid product of carbonisation in carbon dioxide increases the effect of the surface it underlies and so becomes the basic, though not the sole, determinant of reactivity. The extent of this micro-capillary system is indicated by the adsorptive power for carbon dioxide.

Influence of Carbonisation Temperature.—So far, our discussion of adsorption and reactivity has been for clarity based upon comparative results obtained from solid products carbonised at one temperature, 800°, reactivities being all determined at 900°. The influence of carbonisation temperature will now be considered.

Adsorption of carbon dioxide was measured on the solid products obtained by the prolonged vacuum carbonisation of cellulose (filter-paper) at successive temperatures up to 1200° as described in J., 1942, 252. The volumes of carbon dioxide (c.c. at 20° and 760 mm.) adsorbed per g. of solid at 20° were:

Temp.	200°	300°	400°	500°	600°	700°	800°	900°	1000°	1100°	1200°
Vol.	2·5	20·1	27·1	43·9	50·6	57·6	65·3	72·0	74·3	73·4	59·4

Such results are, however, somewhat affected by the time of heating; *e.g.*, the paper coke adsorbed 65·3 c.c. per g. after the prolonged vacuum carbonisation at 800°, 57 c.c. after the 3½ hours' slow carbonisation to 800° (as usually employed in our tests; see Table IV), and 45·5 c.c. after the rapid 20-minutes' carbonisation used in our first preparation of cokes from paper, cotton-wool, sugar, and starch (Table III), suggesting some increase here in the micro-capillary system with time, although, as noted earlier, the filter-paper gave a coke of practically the same adsorption as did the cotton-wool, sugar, or starch, whether the carbonisation had been slow or rapid. The prominent features in the values for adsorption of the paper coke prepared in a vacuum at different temperatures were the sudden rise at 500°, marking the formation of the micro-capillary system as established, the steady and rapid rise between 500° and 900° as the system developed, and the fall from a maximum at 1000°, becoming rapid between 1100° and 1200°, the highest temperature of the carbonisation.

The same rise and fall of carbon dioxide adsorption are reported (" The Solid Products of the Carbonisation of Coal," South Metropolitan Gas Co., 1934, p. 34) as occurring with cokes prepared from a Durham gas-coal, but the maximum was for a coke prepared at 700°, above which temperature adsorption was less and slower. In a few experiments with wood charcoal a higher maximum (about 800°) was obtained. When the coal was carbonised in a tube under vacuum, with a periodical introduction of hydrogen intended to minimise any graphitic formation which would tend to lower adsorption, the attainment of a maximum with subsequent falling away was still just as pronounced.

In the determination of micro-porosity (Table II) made on the solid products throughout the carbonisation range (15—1100°) of anthracite and a meta-bituminous coal, and based on the difference of penetration of water and of mercury, the micro-capillary system which mercury would not penetrate, and that which would be effective in carbon dioxide adsorption, are little different, the limiting diameters being estimated at 6 μ and 12 μ respectively, but the volume of the micro-capillary system is more directly measured by that of the penetrating water. It is seen there that with both anthracite and meta-bituminous cokes this volume reached a maximum at 850° and then shrank.

All these facts point to a rapid growth in the micro-capillary system from 500° upwards during carbonisation and the attainment of a maximum at a temperature which varied somewhat with the material tested. The lowest value for the maximum was 700° for a gas-coal (see South Metropolitan Gas Co., *loc. cit.*), 850° for anthracite and a meta-bituminous coal, and 1000° for cellulose (filter-paper), the last having been subjected to prolonged fractional carbonisation under vacuum. Beyond the maximum, there was a marked shrinkage in volume of the micro-capillary system, which seems, therefore, to be of general occurrence somewhere in the temperature range 800—1200°, although, as noted above, there is no increase in specific gravity.

What may be taken as interesting visual evidence of the shrinkage and a consequent increasing coherence appears in " Photomicrographs of Sulphuric Acid Dispersion of Cokes, carbonised to Various Temperatures " obtained in the South Metropolitan work (Fig. 14 therein). The coke produced at 1030° differed widely from those of lower temperature in giving " a colourless solution containing suspended in it black particles of substantially the same size as the original particles of coke taken for test." This may be taken as due to a consolidation with rising temperature of the carbon structure, opposite in effect to that of the carbon monoxide and finally overcoming it, with consequent diminution in micro-capillarity and reactivity. In approximately the same temperature range the progress of the superficial carbon towards graphite, as demonstrated by equilibrium measurements, will also tend to diminish reactivity during gasification in carbon dioxide, more particularly during its early stages. These two causes of diminishing reactivity, *viz.*, shrinkage of the capillary system and superficial graphitisation, are usually but not necessarily coincident in operation. The results of experiments recorded in Table V illustrate both effects as arising from increasing temperature (and time) of carbonisation.

TABLE V.

Reactivity at 900°, and adsorption by solid products from different temperatures of carbonisation.

A. Filter-paper, $(C_6H_{10}O_5)_n$, infusible. B. Cane-sugar, $C_{12}H_{22}O_{11}$, fusible. C. New Hucknall coal, para-bituminous, semi-fusible.

		Gasification (mins.) in CO_2, and corresponding reactivity.								Mean re-activity.	CO_2 adsorption, c.c./g.	
	Temp.	5.	20.	40.	60.	90.	120.	150.	180.		*V.*	*R.*
A	800°	(4·63)	3·77	2·82	2·37	2·23	2·17	—	—	2·67	56·0	100
	1000 (40 mins.)	2·00	2·00	2·23	2·17	2·00	1·84	—	—	2·04	—	—
	1000 (240 mins.)	(1·18)	1·50	1·55	1·68	1·72	1·53	—	—	1·60	51	85
B	800	0·60	0·60	0·58	0·59	0·59	0·59	0·60	0·60	0·60	58·0	100
	1000 (40 mins.)	(0·38)	0·43	0·48	0·53	0·54	0·56	0·56	0·57	0·52	47	76
	1000 (240 mins.)	(0·30)	0·36	0·41	0·45	0·48	0·50	0·52	0·54	0·47	41	45
C	800	—	—	—	—	—	—	—	—	1·32	27	49
	1400 (25 hrs.)	—	—	—	—	—	—	—	—	0·27	0·7	0

The results for cane-sugar show the fall in reactivity from 0·60 to 0·52 brought about by raising the temperature of carbonisation from 800° to 1000°, and the further fall to 0·47 with a more prolonged time of heating at 1000°. The value after 5 mins.' gasification (0·38; shown in parentheses and not used in calculating the mean

reactivity) shows the lowered reactivity of the surface preheated to 1000° owing to its graphitisation, and this again was more pronounced with the longer exposure at 1000°. Since, however, the gasification of carbon in the whole 120 minutes of the test was only about 8%, the extent of graphitisation was very small, confirming the indications of specific-gravity measurements, although its existence was in full accord with results as obtained in a study of the equilibrium in the reaction $C + CO_2 \longrightarrow 2CO$ and reported above. The adsorption of carbon dioxide, V, was lessened from 58 to 41 c.c./g., and there was a reduced rate of adsorption, R falling from 100 to 45, mainly, it may be assumed, because of a diminished freedom of access through the graphitising surface layer.

The reactivity of the paper coke was much greater (2·67) than that of the sugar coke (0·6). The paper and the sugar contained substantially the same high percentage of oxygen and developed equally the micro-capillary system as indicated by adsorption of carbon dioxide, but the paper did not fuse on carbonisation, and gave a bulkier coke with lower powder-density (0·15 as against 0·4), which presumably meant a greater extent of surface per g. bounding the micro-pores and increasing reactivity. As with the sugar coke, the reactivity of the paper coke and the adsorption both diminished after preheating to 1000°. The reactivity of the paper coked at 800° after 5 mins.' gasification was higher (4·63) than that found subsequently (2·67). This is probably due to the more reactive surface atoms with greater free energy or unsaturated bonds, and is commonly found with unfused material, particularly at lower temperatures. The atoms would form graphitic crystallites on further heating, and the paper coke displayed the lowering reactivity of a graphitising surface (1·18) in the 5-min. sample after 240 mins.' heating at 1000°, although not so markedly as the fused sugar coke. The rate of adsorption was also lowered after this prolonged heating, but again less than with sugar coke. A single example is provided in Table V of the influence of long exposure (25 hours) at a much higher temperature (1400°), above the normal range of our experiments, on New Hucknall (para-bituminous) coal. The reactivity was greatly lowered, from 1·32 to 0·27, and the adsorption almost obliterated, by the combined effects of shrinkage and graphitisation.

Reactivities at High Temperatures.—The comparison of reactivities of the solid products of carbonisation towards carbon dioxide is conveniently made at 900°, but the reactivity has also been determined up to 1500° (Blakeley and Cobb, Gas Research Fellowship, *Trans. Inst. Gas Eng.*, 1934). Roughly, the reactivities were multiplied 100-fold when the temperature was raised from 900° to 1400°. The temperature coefficient of reactivity R_{t+10}/R_t decreased with increasing temperature, but the numerical difference between the reactivities of two solid products increased greatly. A complication in these determinations arises from an alteration in the material itself under the severe heat treatment as gasification proceeds; this was shown to have an appreciable effect but not to invalidate the general relation of results obtained. (The original paper should be consulted for details.) Some typical results are given in Table VI, including tests of materials which at 900° are only slightly reactive.

TABLE VI.

Specific reactivities at different temperatures.

	900°.	1000°.	1100°.	1200°.	1300°.	1400°.	1500°.
Holmside (Durham) coke, carbonised at 920° ...	0·50	2·47	9·2	19·5	52·0	100	—
Same, after 15 mins. at 1400°	0·15	1·10	—	—	—	—	—
Coconut shell, carbonised at 920°	10·5	40·6	137	196	—	—	—
Ceylon graphite	0·04	0·59	3·96	14·0	—	81·2	—
Petroleum coke	—	1·2	—	10·7	—	18·6	29·7
Retort carbon	—	—	2·8	4·2	8·8	—	15·2

Reactivity at Low Temperatures.—From 600° downwards, the reactivity of the solid product of carbonisation towards carbon dioxide has usually fallen to a point at which the method described above for its determination in inapplicable. It becomes more practicable to substitute oxygen (as air) for carbon dioxide and to measure the percentage of the oxygen consumed by the carbonised product as indicated by the expression $100(CO_2 + \frac{1}{2}CO)/(CO_2 + \frac{1}{2}CO + O_2)$, where CO_2, CO, and O_2 represent percentages in the effluent gas (Bolland and Cobb, *J. Soc. Chem. Ind.*, 1933, **58**, 153—159T).

Influence of Inorganic Additions on Reactivity.—It was reported by Lessing and Banks (J., 1924, **125**, 2344) that the course of carbonisation was affected by the presence of certain inorganic salts. This was confirmed in our laboratory by experiments on coal, undertaken primarily to determine the effect as regards sulphur and nitrogen compounds (Marson and Cobb, Gas Research Fellowship, *Trans. Inst. Gas Eng.*, 1925), but amplified by tests on reactivity (*ibid.*, 1926). These were all made on cokes prepared from coal of low ash content (to minimise its possible interference) to which inorganic compounds had been added before carbonisation, and a remarkable heightening of the decomposition of both steam and carbon dioxide was found to result from the addition of soda, lime, or ferric oxide. Moreover, it was demonstrated that almost the same result could be obtained from cokes to which the addition had been made by impregnation with inorganic salts after carbonisation. A method of determining the reactivity towards carbon dioxide of these special and ordinary cokes, which has been used ever since with slight modifications, was reported by Branson and Cobb (*ibid.*, 1927, p. 357) and a necessary working scale connecting a defined reactivity with decomposition of carbon dioxide or steam was published (Key and Cobb, *J. Soc. Chem. Ind.*, 1930, **49**, 439T).

Other work on the various factors influencing the reactivity in gasification of cokes has been carried out in our own and other laboratories and also on a larger scale, but we now deal with experiments on the reactivity of the solid products of carbonisation from an organic substance with and without inorganic additions. Cane-

sugar was chosen as being of known constitution, of negligible original ash content (<0·001%), and as yielding, after fusion and further heating, a coke of rather low reactivity, 0·6. The properties of this coke have already been given in detail. Impregnation of the coke with inorganic additions was carried out at room temperature, soluble salts being used, and penetration of the solution sometimes being aided by evacuation.

In Table VII is shown the influence of adding soda (as sodium carbonate) in gradually increasing quantity, the complete figures being given in this case for the percentage of carbon dioxide decomposed by 5 g. at 900° at periods up to 120 mins. There was a continuous and large rise of carbon dioxide decomposition with the

TABLE VII.

Influence of added Na_2O *on* CO_2 *decomposition*, %.

Additions, %, of Na_2O as Na_2CO_3.	5 mins.	20 mins.	40 mins.	60 mins.	80 mins.	120 mins.	Mean.
Sugar coke (alone)	8·2	7·5	7·2	7·6	7·6	7·8	7·6
+ 0·09 Na_2O	12·3	13·7	14·8	15·8	16·8	16·8	15·0
+ 0·21 Na_2O	20·2	22·3	24·2	24·8	24·9	24·9	23·5
+ 0·35 Na_2O	26·8	28·5	30·3	32·1	32·9	33·7	30·7
+ 0·6 Na_2O	45·2	49·1	49·3	50·9	52·6	49·3	49·4
+ 0·8 Na_2O	62·6	72·0	76·0	65·8	56·2	52·1	64·1
+ 1·0 Na_2O	68·2	69·7	74·8	73·2	67·6	58·9	68·7
+ 1·3 Na_2O	82·0	81·0	74·7	74·6	66·4	56·2	72·5
+ 1·4 Na_2O	86·1	87·2	79·4	73·2	68·1	48·9	73·8

increase of carbonate added. Moreover, if a corresponding table is calculated, each figure being corrected for the carbon gasified during the progress of a test, it is shown that there was a gradual rise in the % of carbon dioxide decomposed as gasification proceeded. This would be expected because of the growing concentration of alkali, particularly with the more rapid rates of gasification.

A comparative survey made with equivalent additions of different inorganic substances, 0·01 g.-mol. of oxide per 100 g. of sugar coke, gave the following descending order of mean reactivity at 900° (Key–Cobb scale): BaO, 13·0; Fe_2O_3, 10·0; Na_2O, 8·8; Li_2O, 7·7; SrO, 6·4; CaO, 3·8; K_2O, 3·4; NiO_2, 3·3; PtO_2, 2·7; Ce_2O_3, 1·7; CuO, 1·5; ThO_2, 1·4; Al_2O_3, MnO_2, MgO, ZnO, and Ag_2O 0·8—0·6; sugar coke 0·6. These results embody the correction for carbon gasified, but the order is not altered thereby.

The most pronounced effects were shown by the strongly electro-positive elements, lithium being the most effective weight for weight. The additions were made by impregnation with dissolved salts, usually carbonate or nitrate, and differences in fusibility, volatility, ease of decomposition and reducibility (as, *e.g.*, with ferric oxide) would tend to invalidate the comparison as one dependent solely on an inherent property of the inorganic element added; for instance, although lithium, sodium, and potassium cokes showed reactivities increasing during gasification, those with calcium, strontium, and barium showed decreasing reactivities, explained by the fact that, whereas the alkaline-earth oxides or carbonates are not fused at 900°, the alkaline carbonates are fused, and on that account would be more closely retained on the changing surface of the carbon during its gasification.

Various explanations of the marked increase in reactivity brought about by some of these inorganic additions were considered. It seemed possible that it might be due to some change in the carbons, brought about in the preliminary heating to 900° with the inorganic additions, before being gasified in the reactivity test; but when sugar coke impregnated with soda (1·4%) was given this pre-heating, it was found that, although only 10% of the soda was removed by extraction with water for 12 hours (Soxhlet) and some remained even after boiling in concentrated hydrochloric acid for a further 24 hours (suggesting some degree of fixation of the soda by the coke), yet the coke residue had a very much lower reactivity than that of a normal 1·4% soda-coke and even lower than that of one made up with the much smaller soda content of the residue after extraction. The enhanced reactivity of the soda-coke cannot then be attributed to change in the carbon during pre-heating. Further evidence was forthcoming from determinations of the repeated adsorption of carbon dioxide by cokes pre-heated as before containing soda and baryta. The following results were obtained:

	V, c.c./g.	*R*.	Reactivity.		*V*, c.c./g.	*R*.	Reactivity.
Sugar coke	47	100	0·6	Sugar coke + BaO ...	49	95	32
Sugar coke + Na_2O ...	49	77	5·4				

Thus the change in total adsorption was insignificant, and that in rate of adsorption was slight, and as there was no appreciable change in micro-structure, the reason for the greatly enhanced reactivity must be sought elsewhere.

Now, Dent and Cobb's experiments with graphite (*loc. cit.*) showed that, although the approach to equilibrium on passing carbon dioxide over graphite at 800° was greatly accelerated by sodium carbonate, yet the equilibrium figure (13·8% of dioxide) was unaltered, so catalysis is indicated. Its mechanism will be treated summarily, since it is still under investigation. A mechanism for carbon dioxide and an inorganic oxide RO may be represented thus:

A { (i) $RO + CO_2 \longrightarrow RO{\cdot}CO_2$; (ii) $RO{\cdot}CO_2 + C \longrightarrow RO + 2CO$ } The result is $CO_2 + C \longrightarrow 2CO_2$, which reaction also occurs directly and independently of catalysis.

The analogous mechanism for steam in its simplest form is:

B { (i) $RO + H_2O \longrightarrow R(OH)_2$; (ii) $R(OH)_2 + C \longrightarrow RO + CO + H_2$ } Here, too, the ultimate result $H_2O + C \longrightarrow CO + H_2$, also occurs directly.

Although the decomposition of the carbonate by carbon as in A (ii) occurs readily below 900° (the temperature of reactivity determination in carbon dioxide) with sodium carbonate (F. J. Dent), and the formation of sodium hydroxide as in B (i) was indicated by an initial fixation of steam at 1000° (the usual temperature of reactivity determination in steam) (A. J. Wilson), yet the application of this explanation to lime and other activating substances offers obvious difficulties, particularly when still higher temperatures are considered at which their carbonates and hydrates cannot exist, but enhancement of reactivity continues.

A possible explanation of the enhanced reactivities may be based on the energy of free electrons, as involved in the catalytic action at the surface of metals, carbon being itself a conductor. The following sequence of elements is in the ascending order of the maximum kinetic energy of their free electrons (Nyrop, *J. Soc. Chem. Ind.*, **1931**, **50**, 752) : K, Na, Li, Ca, Mg, Ag, Al, C, Cu, Zn, Pt, Cr, Fe, Ni, Mn. On comparing that order with the one given above (p. 587) for reactivities induced by the impregnation of salts of the elements, it would appear that, in general, the oxides and salts of those elements possessing electronic energies greatly different from that of carbon were actually more efficient catalysts but, as there explained, disturbing factors enter which cannot be evaluated.

Summary and Conclusions.—This work, following upon the study of the primary gaseous products of carbonisation (J., 1942, 253), is applied to cellulose (filter-paper and cotton-wool), sugar, coals of different types, anthracite, petroleum coke, retort carbon, graphite, etc., and is mainly directed to tracing some properties capable of numerical expression.

(i) The specific gravity, whatever it may be initially and in the first stage of carbonisation, reaches a common value of *ca.* 1·4 at 500° and rises with temperature to 1·8 at 800°, then remains nearly constant at about 1·85 up to 1200°, the highest temperature of our experiments. The steady period, 800—1200°, is marked by the long-continuing emission of hydrogen and carbon monoxide, and this gas, by lying between parallel sheets of graphite crystallites, probably prevents their coalescence and consequent increase of specific gravity. Although all the materials tested have this bulk density from 800° to 1200°, yet a superficial graphitic film is also formed, but is not thick enough to exercise any appreciable influence on the specific gravity. Fundamentally, therefore, the solid product was always the same carbon, over a wide range of temperature for all the materials tested, but differences in physical structure emerged which determine differences in behaviour and appearance.

(ii) The micro-capillarity of the solid product, as indicated by reversible carbon dioxide adsorption at room temperature, or by the difference in specific gravity as determined in mercury and water, increased from a carbonising temperature of *ca.* 500° to a maximum at 800—1000° (according to substance and method of carbonisation) and then diminished. The micro-capillary system so formed was most fully developed in the solid product from a material rich in oxygen, such as cellulose, and became negligible when the material contained little or no oxygen. The following explanation seems applicable. Oxygen left in the solid residue at 400—500°, at which temperature the formation of graphitic crystallites was first prominent, is the agent by which carbon is gasified as oxides, mainly from nuclear carbon in the hexagonal network, by the reaction $R_1OH + R_2H \longrightarrow R_1R_2 + H_2O$, followed by the attack of steam on carbon (see J., 1942, 252), thereby giving rise to a very intimate micro-capillary system.

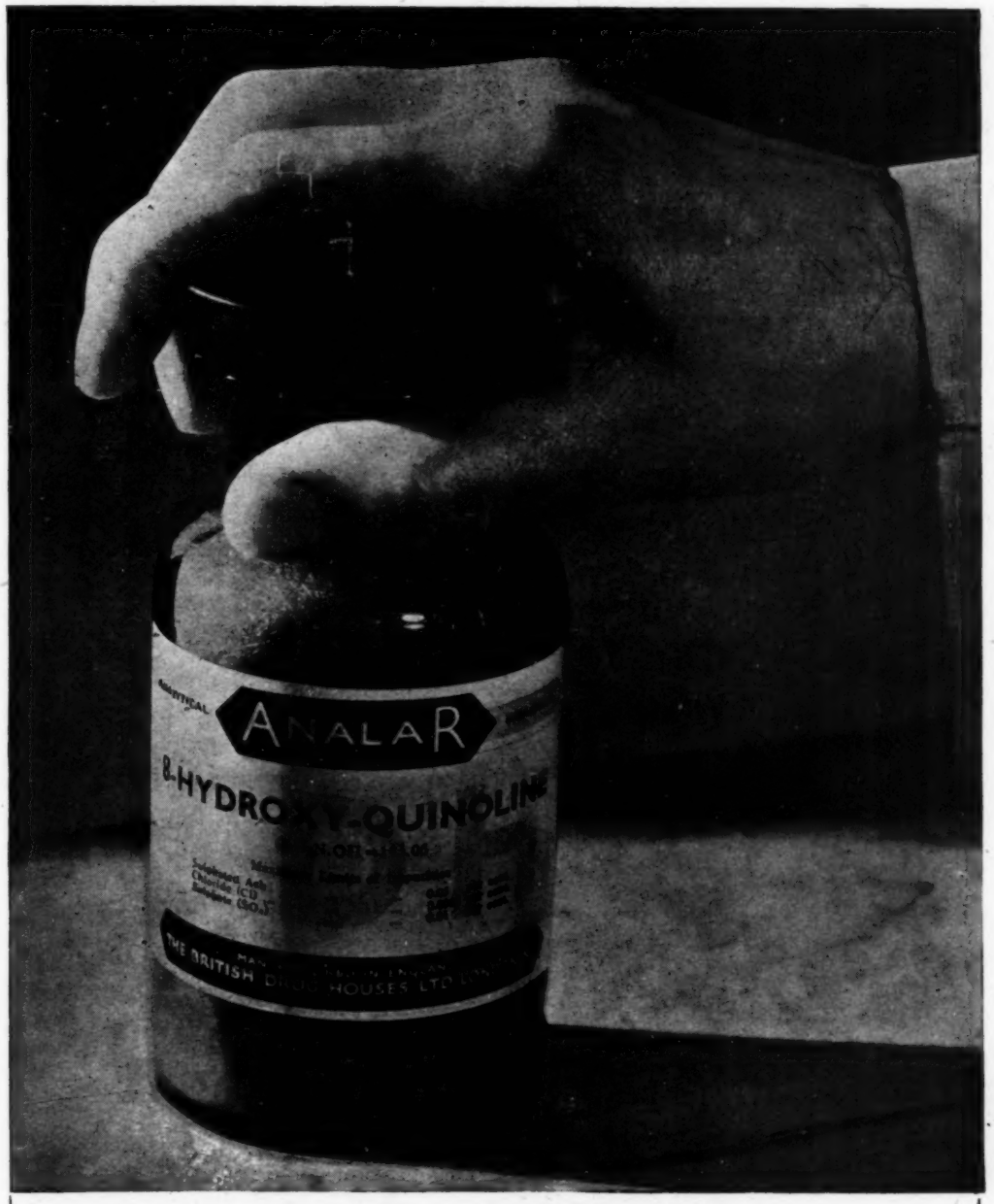
(iii) The reactivity of the solid product towards carbon dioxide at any particular temperature depends on the nature of the carbon, and the extent of surface over which the gas flows, but a primary determinant of the surface effective in gasification is the extent of the underlying micro-capillary system, not because of gas flow through these capillaries (which is very small), but because their terminations at any surface render it so discontinuous and open to attack. In the absence of such a system the surface is comparatively inert. Reactivity therefore depends largely on the oxygen which remains in the solid product at 400—500° and generates the capillary system as the temperature rises further. There is, however, another important factor. When sugar coke was mixed with inert alundum, the extent of the micro-capillary system and the adsorption on coking were unaffected, but the increase of surface bounding the micro-capillaries brought the reactivity up from 0·6 to 2·02, comparable with that of paper coke.

It was found that if a coal was allowed to take up oxygen by prolonged heating in air at 150°, the quantity of oxygen fixed by the coal and the reactivity of the coke rose gradually together. Heating in nitrogen had no such effect although carbon dioxide and water were expelled. Values of oxygen in the original material, and of adsorption, rate of adsorption, and reactivity of the solid products of carbonisation, were obtained for a wide range of substances (Table IV).

It was deduced that, although there was no scientific basis for placing the reactivities of the solid products of carbonisation in the same order as the oxygen contents of the original materials, or as the adsorption or rate of adsorption by the carbonised product, yet there was a causal connection between the oxygen expelled from combination with carbon from 500° upwards, the micro-capillary system (indicated by adsorption) which it generated in the solid product of carbonisation, the surface effective in gasification, and the reactivity.

In the results for the wide range of coals in Table IV, the order of oxygen content, adsorption, and reactivity was nearly the same. This is comprehensible. The greater the previous molecular condensation with loss of easily expelled oxygen (irrelevant to these phenomena), the closer would be the correspondence expected between the oxygen content of materials and the adsorptions (or reactivities) of their cokes. All coals have already undergone such condensation in their formation from vegetation. A comparison after heating to (say) 400° would presumably heighten the degree of correspondence.

(iv) When the temperature of carbonisation was increased, the consequent shrinkage of the micro-capillary



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